Summer November 2014

Stress and Depression during Pregnancy among Hispanic Women: Risk for Adverse Birth Outcomes and the Role of Physical Activity

Kathleen Szegda
University of Massachusetts - Amherst

Stress and Depression during Pregnancy among Hispanic Women: Risk for Adverse Birth Outcomes and the Role of Physical Activity

A Dissertation Presented

by

KATHLEEN SZEGDA

Submitted to the Graduate School
of the University of Massachusetts, Amherst in partial fulfillment
of the requirements for the degree of

DOCTOR OF PHILOSOPHY

September 2014

Department of Public Health
Epidemiology

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Approved as to style and content by:

_____
Lisa Chasan-Taber, Chair

_____
Elizabeth Bertone-Johnson, Member

_____
Penny Pekow, Member

_____
Sally Powers, Member

_____
Edward Stanek, Department Chair
Department of Public Health

ACKNOWLEDGEMENTS

I would like to thank my advisor and Committee Chair, Lisa Chasan-Taber, for her continual support and guidance throughout my doctoral and dissertation process. I would also like to thank my Committee members, Liz Bertone-Johnson, Penny Pekow, and Sally Powers, for the invaluable feedback and insight they provided for my dissertation. Finally, I would like to especially acknowledge that this would not have been possible without the love and support of Agnés, Théo and my parents throughout this process.

ABSTRACT

STRESS AND DEPRESSION DURING PREGNANCY AMONG HISPANIC WOMEN: RISK FOR ADVERSE BIRTH OUTCOMES AND THE ROLE OF PHYSICAL ACTIVITY

SEPTEMBER 2014

KATHLEEN SZEGDA, A.B. CORNELL UNIVERSITY

M.S. GEORGIA STATE UNIVERISTY

M.P.H. EMORY UNIVERSITY

Ph.D. UNIVERSITY OF MASSACHUSETTS

Directed By: Professor Lisa Chasan-Taber

Preterm birth and low birth weight are among the leading causes of infant mortality and morbidity in the United States. Puerto Rican women are at increased risk for these adverse birth outcomes and elevated levels of depression and psychosocial stress during pregnancy when compared to non-Hispanic Whites. Therefore, it is important to understand whether these psychological factors increase risk for these adverse birth outcomes and mechanisms to prevent/reduce depression in this high-risk population.

The first study of this dissertation examined associations between perceived stress during pregnancy and preterm birth, low birth weight, and birth of a small-for-gestational age infant (SGA) in a population of predominantly Puerto Rican women that participated

in Proyecto Buena Salud (PBS), a prospective cohort study. In adjusted analyses, mid-pregnancy perceived stress was positively associated with low birth weight and both early and mid-pregnancy stress was positively associated with preterm birth. In addition, an increase in perceived stress during pregnancy was positively associated with SGA in adjusted analyses. Findings from this study suggest that timing and patterns of exposure to stress are important to consider in screening and prevention efforts.

The second study examined associations between depression during pregnancy and preterm birth, low birth weight and SGA among PBS participants. Early and mid-pregnancy depression was positively associated with SGA in adjusted analyses. Increasing duration of exposure to major depression during pregnancy was also found to increase risk for SGA. No associations were observed between depression and preterm birth or low birth weight. Findings suggest that depression screening and intervention in early pregnancy is important to reduce risk for SGA.

The third study evaluated the association between physical activity and depression during pregnancy in PBS participants. Few associations were observed in prospective analyses. Contrary to expectations, total physical activity was positively associated with depression in some adjusted analyses, likely because the majority of physical activity among participants was non-voluntary (e.g. household/caregiving) and potentially stressful. Findings suggest a protective effect of early pregnancy physical activity on mid-pregnancy depression among women that did not have depression in early pregnancy, though more research is needed to confirm these findings.

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CHAPTER 1

PSYCHOSOCIAL STRESS AND ADVERSE BIRTH OUTCOMES AMONG PREGNANT HISPANIC WOMEN

Introduction

Preterm birth (<37 weeks gestation) and low birth weight (<2500 grams) are among the leading causes of infant mortality and morbidity in the United States.[1, 2] Though rates of these adverse birth outcomes are comparable among Hispanics and non-Hispanic Whites overall, rates vary among Hispanics by country of descent. Puerto Rican women experience higher rates of these adverse birth outcomes than non-Hispanic Whites, with almost double the rate of low birth weight[3] and a 26% higher rate of preterm birth.[4] In addition, Puerto Rican women are disproportionately impacted by the effects of adverse birth outcomes. Disorders related to preterm birth and low birth weight are the leading cause of infant mortality among Puerto Rican women and occur at a rate that is more than double that of non-Hispanic White women. [1] Consequently, it is important to identify risk factors that can be addressed to prevent these adverse birth outcomes in this high-risk population.

Psychosocial stress has been identified as a potential risk factor for preterm birth and low birth weight, or growth restriction during pregnancy.[5] The primary neurobiological mechanisms theorized to explain the association between psychosocial stress and these adverse birth outcomes involve the systems primarily responsible for the body's physiological stress response: the hypothalamic-pituitary-adrenal (HPA) axis, and the sympathetic nervous system. The theories commonly proposed to explain how stress

may lead to early parturition include: (1) elevated corticotrophin releasing hormone (CRH) levels triggering early parturition; and (2) elevated catecholamine levels leading to increased risk of infection and subsequent inflammation triggering early parturition. Theories suggesting how psychosocial stress can lead to growth restriction include prolonged exposure to: (1) elevated catecholamine levels leading to reduced uterine blood flow inhibiting growth; and (2) elevated cortisol levels causing growth restriction. As studies have found that HPA axis regulation and hormone levels during pregnancy may vary by race/ethnicity,[6, 7] it is possible that some of these neurobiological pathways would vary for different racial/ethnic groups.

Behavioral pathways theorized to explain how psychosocial stress may impact preterm birth, low birth weight and SGA primarily focus on increased psychosocial stress leading to an increase in risky health behaviors, such as smoking and inadequate nutrition, or the underutilization of prenatal care. These risky health behaviors and their associations with adverse birth outcomes have also been demonstrated to vary between racial/ethnic groups.[8]

Low birth weight is often used as a measure of growth restriction during pregnancy in studies examining the association between psychosocial stress and low birth weight. However, as it does not take into account gestational age at birth, it includes both infants that are small because they experienced intrauterine growth restriction, and infants that are small because they were born preterm. Consequently, another measure used in studies to assess growth restriction is small-for-gestational-age (SGA) (or intrauterine growth restriction), which is typically defined as less than the 10th percentile for age-specific weight. Though SGA may be considered a more specific measure of growth

restriction, there is concern that it only captures the more extreme end of growth restriction, which is why some researchers have argued for the use of low birth weight.[5]

The studies examining the association between psychosocial stress and these adverse birth outcomes have generally been conflicting. The studies are characterized by variability in the assessment of psychosocial stress, including both the measures used to evaluate stress and the pregnancy period during which stress was assessed, and their categorization of each of the adverse birth outcomes (preterm birth, low birth weight, SGA) making it difficult to compare findings. In addition, some of the measures used to assess psychosocial stress only measure the occurrence of potential stressors (e.g. life events, daily hassles), and do not take into account individual variability in the perception of a given event as stressful, which is determined by an appraisal process that involves assessment of a stressor as threatening/demanding in light of available coping resources (e.g. coping resources). Also, these measures only focus on specific types of stress and do not take into account all sources of stress. Many of the studies had other limitations, including: (1) small sample sizes limiting power to detect effects, (2) retrospective designs making it difficult to determine temporality, (3) lack of consideration of confounders, (4) assessment of stress at a single time point during pregnancy, and (5) lack of consideration of other psychosocial factors as potential confounders or effect modifiers. Finally, previous studies have focused primarily on non-Hispanic White women or Black women with very few, if any, focused on Hispanic women.

Therefore, this study extends the prior literature by prospectively examining the association between psychosocial stress and preterm birth, low birth weight, and SGA, among pregnant Hispanic women that are primarily Puerto Rican. To our knowledge,

this is the first study to examine this association in a Puerto Rican population. Stress was assessed with the Perceived Stress Scale, a validated instrument that assesses global levels of stress and takes into account individual variation in the appraisal of potential psychosocial stressors as "stressful," and was assessed at multiple time points during pregnancy. Both pattern of psychosocial stress and cumulative exposure during pregnancy were examined. A number of sociodemographic, acculturation, behavioral, physical and mental health factors were considered as potential confounders. In addition, depression and anxiety were examined as potential effect modifiers. Finally, the association between psychosocial stress and preterm birth by subtype and gestational age of preterm birth was assessed as etiologies may differ and psychosocial stress may only increase risk for some types of preterm birth.

Physiological Mechanisms

Neurobiological Mechanisms

Several neurobiological mechanisms involving the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system have been proposed to explain how psychosocial stress may contribute to preterm birth, low birth weight, and SGA. The theories primarily focus on corticotrophin releasing hormone (CRH), cortisol and catecholamines as the agents initiating the physiological processes that lead to these adverse birth outcomes.

Preterm Birth

The most commonly discussed theory as to how psychosocial stress may lead to preterm birth proposes that increased levels of CRH released in response to psychosocial stress initiates early parturition.[9] Though the mechanisms leading to parturition are not thoroughly understood, CRH is thought to be a component of the complex process initiating birth. In term pregnancy, CRH levels of primarily placental origin rise over the course of pregnancy, and these increased levels are thought to play a role in the initiation of parturition. When experiencing elevated levels of psychosocial stress, levels of CRH may rise prematurely and lead to the early onset of parturition. Some studies have found increased levels of CRH among women with preterm births as compared to term births.[10,11]

Another theory suggests that stress increases the risk for infection,[12] which is one of the major risk factors for preterm birth.[13] Infections lead to inflammation, which is another factor involved in the initiation of parturition in term pregnancy.[13] During a stress response, cortisol, norepinephrine and epinephrine are released by the body and have been demonstrated to modulate the immune system by suppressing innate immune system factors leading to an exaggerated adaptive immune system response.[9] As the adaptive immune response is less effective at preventing infection than the innate immune response, this shift increases risk for infection and subsequent inflammation that can trigger early parturition.

Low Birth Weight and SGA

Proposed physiological mechanisms describing how psychosocial stress may increase risk for low birth weight and SGA focus on how chronic exposure to psychosocial stress during pregnancy may increase the risk for growth restriction, which includes both low birth weight and small-for-gestational age infants. However, these theories are not as clearly defined as those for preterm birth.[5] One theory suggests that norepinephrine released in response to psychosocial stress leads to reduced uterine blood flow and subsequent nutritive delivery to the fetus.[9, 14] Therefore, under chronic exposure to psychosocial stress, this reduced blood flow could lead to fetal growth restriction. A second theory suggests that elevated maternal cortisol levels that occur in response to psychosocial stress inhibit fetal growth.[5] Some animal research studies support this theory as they have found that exposure to high levels of glucocorticoids affects fetal growth.

Racial and Ethnic Differences in HPA Axis Regulation

Some studies examining HPA hormone levels during pregnancy by race/ethnicity have found differences in HPA axis regulation by race/ethnicity. For example, some have found that Hispanic women and Black women have lower levels of CRH and different patterns of release of cortisol and CRH over the course of pregnancy when compared to non-Hispanic White women.[6, 15-17] Also, racial/ethnic differences in the effect of cumulative stress on hormone levels during pregnancy have been observed with one study finding that cumulative stress was associated with decreased cortisol levels and

daytime pattern of release among pregnant Black women, but not Hispanic women.[7] These studies suggest the possibility that there may be racial/ethnic differences in HPA axis function during pregnancy. In a review of the literature, Kramer suggested that these differences in HPA axis function may be a result of chronic stress experienced over the lifetime by some racial ethnic groups (e.g. poverty, limited access to resources, discrimination) with high levels of chronic stress exposure associated with both lower CRH levels in mid-pregnancy and increased risk due to elevated stress levels.[18] As some studies have shown that racial differences persist after adjusting for some of the likely sources of chronic stress experienced by some racial/ethnic groups, such as socioeconomic status,[19] more research is needed to better understand these relationships.

Behavioral Mechanisms

Behavioral mechanisms have also been proposed to explain how stress may increase risk for preterm birth, low birth weight and SGA. Increased stress during pregnancy is associated with an increase in unhealthy behaviors, such as smoking and inadequate nutrition, both of which have been identified as potential risk factors for preterm birth and growth restriction.[11, 20] In addition, stress may impact utilization of prenatal care and adherence to healthcare provider recommendations during pregnancy, which are other potential pathways by which stress may increase risk for adverse birth outcomes. Prevalence of these unhealthy behaviors and their impact on adverse birth outcomes vary across racial/ethnic groups, which may, in part, explain differences in rates of these birth outcomes among different racial/ethnic groups.[8]

Prior Epidemiological Research

Preterm Birth

Studies examining the relationship between psychosocial stress during pregnancy and preterm birth have been conflicting. Of the 36 English language studies identified that examined the association between stress and preterm birth, or gestational age, 17 found a positive association between stress and preterm birth (odds ratio range=1.06-2.41), or decreased gestational age at birth, and 19 found no association. The majority were cohort studies, fifteen of which found a positive association, and seventeen which had null results. The remaining studies identified consisted of two case-control studies and two cross-sectional studies. The vast majority of studies examined stress at a given timepoint in pregnancy with very few examining the effect of stress over the course of pregnancy.

In a widely cited cohort study, Dole et al. assessed the effects of life event stress, perception of racial/gender discrimination, and perception of neighborhood safety during pregnancy on preterm birth.[21] The study included 1,962 predominantly White, pregnant women (58% White, 36% African-American, 6% Other) recruited through prenatal clinics. Information on life events stress, perception of racial/gender discrimination, and perception of neighborhood safety was collected through a validated instrument, the Life Experiences Survey, between 24 and 30 weeks gestational age. Preterm birth (<37 weeks gestation) was determined via hospital records. Women that experienced high counts of negatively perceived life events had almost double the odds of preterm birth compared to women experiencing low counts (OR=1.8, 95% CI=1.2, 2.7) after adjusting for a variety of potential confounders. In addition, women who experienced perceived racial

discrimination had 40% increased odds of preterm birth (OR=1.4, 95%CI=1.0, 2.0). No relationship was found between perceptions of gender discrimination or neighborhood safety on preterm birth. Also, life events stress was not associated with spontaneous or medically indicated preterm birth when analyzed separately.

Glynn et al conducted one of only two studies to assess patterns of stress and risk for preterm birth or decreased gestational age.[22] Glynn theorized that patterns of stress may be important to examine as studies suggest that women tend to experience a blunted physiological response to stress over the course of pregnancy and those that experience an increase in stress may be particularly susceptible to the effects of stress or have a dysregulation in the parturition process resulting in increased risk for preterm birth. This study is also one of few studies to examine the association between psychosocial stress and preterm birth in a racially/ethnically diverse population that included Hispanic women (23% Hispanic, 14% African-American, 48% non-Hispanic White, 15% Other). The study examined the association between perceived stress and preterm birth among 415 women receiving prenatal care at a large medical center.[22] Perceived stress was assessed at 18-20 and 30-32 weeks gestation using a modified version of the 10-item Perceived Stress Scale (PSS-10).[23] Preterm birth (<37 weeks gestation) information was obtained through patient medical records. Perceived stress was not found to be associated with preterm birth at either time point (18-20 wks GA: r=0.01, p-value not shown; 30-32 weeks GA: r=0.09, $p<0.1$), though the analysis was limited to unadjusted correlation analyses. However, women that experienced an increase in stress from 18-20 to 30-32 weeks had 3 times the odds of preterm birth compared to women that did not experience an increase, after adjusting for parity and race/ethnicity (OR=3.08, 95%

CI=1.51, 6.28). Change in stress remained statistically significantly associated with preterm birth after adjusting for level of stress at 18-20 weeks and change in anxiety over pregnancy. When examined as a continuous variable, change in the PSS-10 score was not associated with preterm birth in regression analysis. Similarly, Ruiz et al. found that measures of perceived stress in mid- and late pregnancy were not associated with gestational age, however, decreases in perceived stress scores were associated with greater gestational length. In this case, this association was found when assessing perceived stress as a continuous variable, and thus greater decreases were associated with longer gestational length.[24] These studies suggest that patterns of stress during pregnancy may be important to consider in studies attempting to elucidate the role of stress on preterm birth.

As illustrated by these studies, and characteristic of studies assessing the relationship between psychosocial stress and preterm birth in general, there is wide ranging variability in the: 1) measures used to assess and operationalize psychosocial stress (e.g. life events vs. perceived stress, timepoint specific stress vs. change in stress), and 2) timeframe during which psychosocial stress was assessed. This variability in study design must be considered when interpreting results as it likely contributes to the conflicting findings in the literature. For example, the majority of studies used life events to measure or operationalize stress (e.g. life events inventory, major catastrophe). Objective counts or occurrence of major/catastrophic life events do not take into account individual variability in the appraisal of events as stressful, which is based on an individual's assessment of an event as demanding, or threatening, and available coping resources (e.g. social support). Though some studies attempt to account for this by

assessing perception of the events as stressful or adjusting for social support, many do not. In addition, they only measure the extent to which the events of interest impact the outcome, and do not take into account other life experiences that may contribute to one's overall level of stress experienced, or the possible synergistic effect of multiple stressful experiences. In comparison, the Perceived Stress Scale is a global measure of stress that assesses the extent to which one's life experiences are perceived as stressful, thus inherently taking into account mediators of the appraisal process (i.e. assessment as threatening, coping resources) and all sources of stress.[25]

Timing of exposure to psychosocial stressors has also been discussed as an important factor that may modify the effect of stress on preterm birth. For example, some have argued that stressful life events experienced during the first trimester are more likely to be related to preterm birth as opposed to stress during other trimesters as studies have demonstrated that the physiological stress response diminishes as pregnancy progresses.[5, 26]

Also likely contributing to conflicting findings is the variability in assessing preterm birth. Some studies have examined stress in preterm birth overall, whereas others have examined subtypes of preterm birth (spontaneous vs. medically indicated). This is important to consider as some have argued that psychosocial stress is more likely to be related to spontaneous preterm birth as medically indicated preterm births have different etiologies;[11] though, studies specifically focusing on spontaneous preterm births have been conflicting.[21, 27, 28] Also, some studies have chosen to look at gestational age as a continuous variable[24, 29-32] while others have chosen preterm birth cut-points that are

different than the commonly used preterm birth definition of less than 37 full weeks gestation.[27]

Limitations occurring in a number of studies included: 1) small sample sizes in some studies that did not find an association, indicating that they might not have had enough power to detect an effect;[29, 30, 32-34] 2) retrospective or cross-sectional data collection making it difficult to ascertain the temporality of the relationship between stress and pre-term birth and also increasing the potential for recall bias[35-38]; and 3) lack of adjustment for confounders.[24, 38-40] In addition, as discussed above, the vast majority of studies only assessed psychosocial stress at one timepoint during pregnancy, with only two studies assessing pattern of psychosocial stress during pregnancy.[22, 24] None of the identified studies assessed the duration of exposure to psychosocial stress during pregnancy on preterm birth, which may be important to examine as this could result in sustained elevated exposure to stress hormones. Most studies also did not include other potential co-morbid psychosocial factors, such as depression and anxiety, as potential confounders or effect modifiers. Among those that did, only one study assessed effect modification, finding no statistically significant effect modification.[21] The others that accounted for the effects of other psychosocial factors only assessed them as confounders.[22, 28, 34] Finally, the studies were primarily conducted among non-Hispanic White or Black populations with no identified studies that focused on a Hispanic or Puerto Rican population.

Given these limitations and the variability in study design (e.g. differing methods of assessment of psychosocial stress), the studies do suggest a positive effect of psychosocial stress on preterm birth as a number of the studies finding null associations

that examined preterm birth as the outcome are limited by small sample size and use of cross-sectional and retrospective design.

Low Birth weight (LBW)

Studies examining the relationship between psychosocial stress and low birth weight have also been conflicting. Of the 19 English language studies identified, 12 found a positive association between stress and low birth weight (odds ratio range=1.08-1.74), or decreased birth weight, and 7 found no association. Similar to the studies examining stress and preterm birth, the majority were cohort studies (15 cohort, 2 cross-sectional, 2 case-control). The studies suggest a positive association between psychosocial stress and low birth weight as the majority of studies finding a positive association focused on the effect of psychosocial stress on low birth weight, whereas, the majority finding a null association focused on birth weight as a continuous outcome. Similar to the studies assessing the effect of stress on preterm birth, the vast majority of studies assessing the association between stress and low birth weight examined the effect of stress at a single timepoint and had many similar limitations.

In a widely cited cohort study, Copper et al. examined the impact of stress during pregnancy on low birth weight among 2,593 predominantly Black women.[27] Participants were recruited from obstetric units at ten centers. Stress was assessed between 25 and 29 weeks gestation using the stress subscale of the Abbreviated Scale for the Assessment of Psychosocial Status in Pregnancy. Low birth weight (<2500 grams) was ascertained from patient medical records. For each unit increase in stress reported by the participants, there was an 8% increase in the odds of low birth weight (OR=1.08, 95%

CI=1.01-1.15), after adjusting for a variety of potential confounders. Among the other identified cohort studies, seven found a positive relationship between stress and preterm birth or decreased gestational age, and seven found no association.

In the only identified study to examine the association between stress and low birth weight in a Hispanic population, Campos examined the relationship between perceived stress and low birth weight among 99 Hispanic and 166 non-Hispanic White women referred for prenatal care at two large urban medical centers.[41] The vast majority of Hispanic participants were of Mexican descent. Perceived stress was assessed at 24 to 26 weeks gestation using a modified version of the 12-item Perceived Stress Scale. Low birth weight was determined using participants' medical records. Perceived stress was not correlated with low birth weight among foreign-born Hispanic ($r=0.03$, p-value>0.10), U.S. born Hispanic ($r=0.04$, p-value>0.10) or non-Hispanic White women ($r=0.14$, p-value>0.10). Limitations of this study include the small sample size when examining this association in Hispanic women, and the lack of consideration of potential confounders, such as parity. As parity may be positively associated with psychosocial stress level and is inversely associated with low birth weight, it could lead to negative confounding, and thus, an underestimate of effect.

As demonstrated by these two studies, similar to the assessment of the effect of stress on preterm birth, there was variability in the measurement of stress in studies examining its effect on low birth weight, with a number using life events or daily hassles to assess stress, others using perceived stress, and yet others using a variety of additional measures (e.g. social readjustment scale, assessment of stressful domains). In addition, there was variability in the measurement of low birth weight with a number of studies

examining birth weight as a continuous variable[29-31, 42-44] rather than the dichotomous low birth weight outcome.

Similar limitations discussed above for stress and preterm birth also existed in many of the studies assessing the relationship between stress and low birth weight, including: (1) small sample sizes,[30, 33, 41] (2) cross-sectional and retrospective study designs,[37, 45-47] (3) use of unvalidated instruments to assess psychosocial stress,[44, 46, 47] and (4) lack of adjustment for important confounders.[33, 41, 47, 48] In addition, few studies assessed psychosocial stress at more than one timepoint in pregnancy[41, 49] and none assessed the effect of pattern of psychosocial stress over pregnancy on low birth weight. Also, only several studies adjusted for anxiety or depression[42-44] in their analysis, and none assessed potential effect modification by these psychosocial factors. Finally, only one identified study examined this relationship in a Hispanic population, with the study focusing primarily on Mexican women and limited by a small sample size and lack of consideration of potential confounders.[41]

Small-for-Gestational Age

Studies examining the relationship between stress during pregnancy and SGA have tended not to find an association. Of the fourteen studies that have been conducted, 12 did not find a relationship between stress and SGA, while 2 found a positive association (stress continuous OR=1.02; severe life event OR=1.25). Although all but one study was a cohort study, as will be discussed below, many of these studies had important limitations. In addition, the majority were conducted in European non-Hispanic White populations.

In one of the identified studies finding a positive association between stress and SGA, Paarlberg et al. examined the association between daily stressors and SGA.[50] In this cohort study, 396 nulliparous women were recruited from obstetric clinics in Amsterdam. Number of daily stressors was assessed in the first, second and third trimester of pregnancy. SGA was determined via medical record using two methods: (1) customized percentiles adjusted for parity, infant gender, and maternal height, weight and ethnic group, and (2) birth weight for gestational age standards based on the Dutch population. For each unit increase in number of daily stressors experienced during the 1st trimester, women experienced a 4% increase in odds of SGA infants born less than the 5th customized percentile (OR=1.04, 95% CI=1.01, 1.07) after adjusting for a variety of confounders. There was no association between unit increase in number of daily stressors in the second and third trimesters and SGA using this definition (2nd trimester: OR=1.00, 95% CI= 0.97,1.03; 3rd trimester: OR=1.02, 95% CI=0.99, 1.05). In addition, there was no association between daily stressors and SGA when the SGA cut-off was set at the 10th customized percentile. Women with low perceived severity of daily stressors in early pregnancy were less likely to have an SGA infant born smaller than the 5th or 10th customized centile compared to women with high perceived severity, though the effect was not statistically significant. However, the effect became more pronounced and was statistically significant when using the Dutch birth weight standards to identify SGA infants born smaller than the 10th percentile (OR=0.41, 95% CI=0.17,0.97).

In one of the few identified studies conducted in a racially/ethnically diverse population, Goldenberg et al. examined the association between stress and SGA among 1,545 low-income women (69% Black, 31% White) delivering at the University of

Alabama Hospital.[51] Maternal stress was assessed using a 4-item questionnaire at 24-26 or 30-32 weeks gestational age. SGA was defined as infants with birth weights less than the 15th percentile for race, infant sex, and parity based on Alabama standards. There was no association between high stress levels and SGA after adjusting for smoking and maternal education, age, height and weight (high vs. low stress OR=1.36, 95% CI=0.93,1.99). An important limitation of this study was the use of an unvalidated instrument to assess stress.

As can be seen by these studies, there was similar variability in the assessment of stress when examining its relation with SGA as compared to the other adverse birth outcomes. In addition to the methods of assessing stress used in the above studies, some studies used measures of perceived stress[49, 52-54] while many studies used life events[55-60] to evaluate stress. There was also variability in the categorization of SGA with some studies identifying SGA based on standards for birth weight specific to age,[27, 52] others taking into account additional factors that affect birth weight including sex and parity,[61] and yet others using percentile cut-points to define SGA that were different than the commonly used value of less than 10% for gestational age.[50, 51, 58, 59]

There were a number of limitations among the studies with null findings that could have led to these results, including small sample sizes with limited power to detect associations,[53, 57, 61] and retrospective data collection, which could lead to bias due to differential recall of stress based on outcome status.[54] In addition, many of the studies were subject to potential nondifferential misclassification of exposure of stress, including: (1) use of event or daily hassles inventories with no consideration of coping resources, such as social support,[56, 57, 61] (2) use of unvalidated instruments,[51] and (3)

assessment of specific domains of stress, such as relational stress, thus not taking into account other potential sources of stress.[58] Finally, an important limitation was that the majority of studies took place in European populations[50, 52, 55, 57-61] with very few taking place in racially/ethnically diverse populations, and none that were identified that examined the relationship between stress and SGA in a Hispanic or Puerto Rican population.

Summary

Preterm birth and low birth weight are among the leading causes of infant mortality in the United States.[1] Puerto Rican women are particularly at risk for both increased incidence of these adverse birth outcomes and increased rates of infant mortality associated with these outcomes. Therefore, it is important to identify risk factors that can be addressed to allow the development of appropriate prevention strategies in this high-risk population.

Psychosocial stress has been identified as a potential risk factor for preterm birth, low birth weight, and SGA. Several neurobiological theories have been proposed to explain how stress may lead to these adverse birth outcomes, including elevated levels of CRH and catecholamines triggering processes that may lead to early parturition, and cortisol and catecholamines leading to fetal growth restriction. Suggested behavioral pathways include increased stress levels leading to unhealthy behaviors (e.g. smoking, inadequate nutrition) or inadequate prenatal care, which in turn, increases risk for these adverse birth outcomes.

Studies conducted examining the relationship between stress and these adverse birth outcomes have generally been conflicting. Limitations of these studies include: heterogeneity in the operationalization of stress, use of unvalidated instruments to assess stress, lack of consideration of the stress appraisal process, measurement of stress at a single timepoint during pregnancy, lack of control for confounding, and lack of consideration of other psychological factors. In addition, these studies have focused predominantly on non-Hispanic White or Black women with the one study focusing on Hispanic women (primarily Mexican) limited by small sample size.

Our study examined the relationship between stress and preterm birth, low birth weight and small-for-gestational age among Hispanic women (predominantly Puerto Rican). We assessed stress using a validated instrument, the 14-item Perceived Stress Scale (PSS-14), which takes into account all sources of stress and the stress appraisal process. The association between stress levels at different time points during pregnancy and adverse outcomes was assessed, in addition to the effect of patterns of exposure to stress. We also took into account other psychosocial factors and assessed whether the effect of stress varied for outcome-specific subcategories (e.g. medically indicated preterm birth vs. spontaneous preterm birth).

Specific Aim and Hypotheses

Specific Aim: To examine the association between psychosocial stress and adverse birth outcomes during pregnancy among Hispanic women

Hypothesis a: Psychosocial stress during pregnancy is positively associated with preterm birth

Hypothesis b: Psychosocial stress during pregnancy is positively associated with low birth weight

Hypothesis c: Psychosocial stress during pregnancy is positively associated with small-for-gestational age

Methods

Study Design and Population

The study examined the association between psychosocial stress and adverse birth outcomes during pregnancy using data from Proyecto Buena Salud (PBS), a prospective cohort study conducted from 2006-2011. The study was based at a large tertiary care center in Western Massachusetts, Baystate Medical Center, which has approximately 4,500 deliveries per year and serves an ethnically, socioeconomically diverse population. Details about the study design have been published previously.[62] PBS was approved by the University of Massachusetts, Amherst and Baystate Medical Center Institutional Review Boards.

Briefly, women were recruited in early pregnancy at prenatal care visits (up to 20 weeks gestation). All participants read and signed a written informed consent approved by the Institutional Review Boards at the University of Massachusetts-Amherst and Baystate Medical Center. Interviews were conducted by trained, bilingual interviewers in English or Spanish depending on patient preference. Eligibility for PBS was restricted to women of Puerto Rican or Dominican Republic ancestry, specifically, women that were either: 1) born in Puerto Rico or the Dominican Republic themselves; or 2) had at least one parent or both grandparents born at either of these two locations. As PBS was initially conducted to assess the relationship between pregnancy factors and gestational

diabetes, other exclusion criteria included: multiple gestation; history of diabetes, hypertension, heart disease or chronic renal disease; less than 16 years of age or greater than 40; and current use of medications thought to adversely affect glucose tolerance. Additionally, participants with antepartum fetal deaths were excluded. Women were interviewed at three timepoints during pregnancy: (1) early pregnancy (≤18 weeks gestation), (2) mid-pregnancy (19-26 weeks gestation), and (3) late pregnancy (>26 weeks gestation). For some women, interviews were not able to be conducted for all of the pregnancy periods.

At the initial interview, participants completed a perceived stress questionnaire and provided information on sociodemographic, acculturation, behavioral, and other psychological factors. Information was updated at the two subsequent interviews. Medical records were abstracted after delivery for information on medical history, clinical characteristics of the pregnancy, and birth outcomes. Among the PBS participants, 1,266 met the study inclusion criteria and had information on perceived stress and the adverse birth outcomes of interest. Women were included if they had information on perceived stress from at least one pregnancy period. Eight hundred and sixty-two participants had information on perceived stress in early pregnancy, 794 in mid-pregnancy, and 766 in late pregnancy.

Assessment of Perceived Stress

Perceived stress during pregnancy was assessed at each interview in English or Spanish using Cohen's 14-item Perceived Stress Scale (PSS) depending on participant preference.[23] The PSS assesses levels of global perceived stress. The instrument is

theorized to inherently account for components of the appraisal process, including both an individual's assessment of potential psychosocial stressors as demanding, or threatening, and the availability of potential coping resources (e.g. social support). The PSS was designed to assess the extent to which an individual feels that their life is "unpredictable, uncontrollable, and overloaded" as these have been found to be the primary aspects of the experience of stress.[25] Examples of questions on the PSS include, "How often have you felt that you were unable to control the important things in your life?" and, "How often have you felt confident about your ability to handle your personal problems?" Responses are on a 0 to 4 scale with negatively worded items ranging from "never"(0) to "very often"(4) (first example above) and positively worded items reverse scored (second example above). Scores for each question were summed resulting in possible total scores from 0 to 56 with higher scores indicating higher levels of stress. Imputation was used for the PSS and other psychological measures included in this study (depression, anxiety) if participants were missing fewer than 10% of items on the given scale.[21] Imputation consisted of replacing the missing value(s) with the participant's average score of the nonmissing items for the given scale. For the PSS, a score was imputed if the participant was missing the value for one item on the PSS. Total stress scores were analyzed continuously and categorically as quartiles.

In addition, composite variables were created between stress and depression (not high stress/not probable major depression, not high stress/probable major depression, high stress/probable major depression, high stress/probable major depression) and stress and anxiety (not high stress/not high anxiety, not high stress/high anxiety, high stress/not high anxiety, high stress/high anxiety) to examine how anxiety and depression may affect

the associations between stress and the adverse birth outcomes. Depression and anxiety were assessed using the Edinburgh Postnatal Depression Scale[63] and the Spielberger State-Trait Anxiety Inventory (STAI),[64] respectively. The EDS is a 10-item scale with scores for each item ranging from 0-3 with total scores ranging from 0-30 and scores greater or equal to 15 indicative of probable major depression. [65] The STAI consists of a trait and state anxiety scale, each consisting of 20 items scored from 1-4, with higher scores indicating higher levels of anxiety. The STAI was used to assess trait anxiety in early pregnancy and state anxiety in mid- and late pregnancy. STAI scores were categorized into quartiles. Participants were categorized as having "high" levels of stress or anxiety if their score for the given scale was in the top quartile of participant scores for that time period. All other women were categorized as having "not high" levels of the given psychological measure.

Finally, the effects of patterns of perceived stress on adverse birth outcomes was assessed by examining change in stress scores during pregnancy and duration of exposure to elevated levels of stress. Change in stress score was examined continuously as the difference between the later pregnancy period PSS score and the early pregnancy score, as a well as dichotomously, comparing women with no decrease in PSS score during the course of pregnancy to those women that experienced a decrease. Duration of exposure was examined by assessing the number of pregnancy periods that a participant reported high levels of stress across two pregnancy periods (e.g. early to mid-pregnancy, mid-to-late pregnancy). Duration of exposure to high stress could not be assessed across all three pregnancy periods due to the limited number of participants with PSS information for all three pregnancy periods.

The PSS is a validated instrument that has been found to have adequate internal consistency (Cronbach's alpha= 0.75)[23] and test-retest reliability (r=0.55-0.85).[25] PSS scores have been found to be correlated with other measures of stress, including stress experienced during an average week (r=0.36) and number of life events experienced (r=0.30), providing evidence of the scale's construct validity.[23] Though PSS scores have also demonstrated a high correlation with the Centers for Epidemiologic Studies Depression Scale (r=0.65-0.76), they have also been found to measure a different, independent construct.[25] The European Spanish version of the Perceived Stress Scale has been validated in a population in Spain and demonstrated good internal consistency (Cronbach's alpha=0.81), test-retest reliability (r=0.73), and sensitivity as evidenced by PSS score trends comparable to perceived stress trends previously identified (e.g. higher stress among females, decreasing stress with increasing age).[66]

The PSS has been referred to by some as a chronic measure of stress.[11] This is supported by findings in a study by Kalra et al., which found that hair cortisol levels during pregnancy were positively significantly associated with perceived stress levels.[67] Hair cortisol has been used in primate research as a biomarker of chronic stress and has recently been shown to be a reliable biomarker of extended cortisol release in pregnant woman.[68, 69] Conversely, studies have had mixed findings when examining the PSS' association with plasma and urine hormone levels, which are biomarkers for the acute stress response.[70-72]

Assessment of Adverse Birth Outcomes

Preterm births are those occurring prior to 37 full weeks of gestation.[73] Cases of preterm birth were identified through medical record abstraction by a trained abstracter. Cases were diagnosed by the hospital obstetricians based on their best clinical estimate, which was typically determined by: (1) ultrasound if available, and (2) last menstrual period when ultrasound information was not available. Information on gestational age at delivery and type of preterm birth was also collected through medical record abstraction. Type of preterm birth consisted of medically indicated and spontaneous preterm births. Medically indicated births are those births in which the physician initiates the labor and delivery process, and spontaneous births are those in which labor occurs spontaneously and include preterm labor or preterm premature rupture of the membranes (PPROM). Based on gestational age at delivery, preterm births were categorized as early (<34 weeks) and late (34-36 weeks). The study obstetrician confirmed all cases of preterm birth and their associated gestational age and preterm birth type.

Low birth weight infants were those with a birth weight less than 2500 grams at birth. SGA was defined as a birth weight less than the 10^{th} percentile for gestational age.[73] Birth weight was assessed by nursing staff using calibrated scales immediately following birth. Information on birth weight was abstracted from the medical record and was used to identify low birth weight infants. This birth weight information and the gestational age information identified above was used to determine SGA case status using gestational age-specific infant weight reference values from a population-based Hispanic sample.[74]

Confounders

A number of sociodemographic, acculturation, behavioral, and physical and psychological factors were assessed as covariates. Information on sociodemographic and acculturation covariates was primarily obtained at the initial pregnancy interview. Sociodemographic covariates included maternal age, education level, income and whether the study participant was living with a partner. Level of acculturation covariates included 1) birthplace of participant, parents, and grandparents, and 2) overall degree of acculturation, which was assessed via the Psychological Acculturation Scale (PAS).[75] The PAS is a 10-item scale with responses ranging from 1-5 with lower scores reflective of a Hispanic/Latina orientation and higher scores indicative of an Anglo-American orientation. Average scores less than 3 were categorized as low acculturation and those greater than 3 as high acculturation. Behavioral factors assessed included smoking and alcohol consumption; pre-pregnancy data on these behavioral factors was collected in addition to pregnancy data at each interview.

Physical and health history factors were obtained by self-report during the initial interview and through medical record abstraction and included: pre-pregnancy weight, height, history of preterm delivery, parity, and history of intrauterine growth restriction. BMI was calculated using reported height and weight. A variable indicating history of preterm delivery or intrauterine growth restriction was created for inclusion in the low birth weight and SGA analyses. In addition, information on antidepressant use during pregnancy was obtained. Women were identified as taking antidepressants if 1) the electronic medical record indicated that they had reported taking antidepressants during

their prenatal visits, or 2) the patient prescription database indicated that they were prescribed antidepressants during pregnancy.

Psychological covariates assessed included depression and anxiety, which were evaluated at each interview via the Edinburgh Postnatal Depression Scale[63] and the Spielberger State-Trait Anxiety Inventory (STAI),[64] respectively.

Data Analysis

The distributions of early, mid- and late pregnancy PSS scores and each of the adverse birth outcomes (preterm birth, low birth weight and SGA) were assessed. Mean PSS scores across pregnancy were determined by 1) calculating the mean PSS score for each participant, and 2) calculating the mean of the participant mean scores. The frequency distribution of preterm births was examined for all preterm births, in addition to the preterm birth subcategories of type (spontaneous vs. medically indicated) and gestational age (early, late).

Bivariate analyses were conducted to examine the associations between covariates and 1) perceived stress, and 2) each of the adverse birth outcomes. When examining the association between perceived stress and the time varying covariates assessed throughout pregnancy, which included the behavioral factors (smoking, alcohol consumption) and the other psychological measures (anxiety, depression), the value of the time varying covariate from the same pregnancy period as the stress measure was used. Trait anxiety was examined when assessing associations with early pregnancy stress because a measure of early pregnancy state anxiety was not available. Chi-square tests, t-tests, and ANOVA were used as appropriate to evaluate associations of participant characteristics

with perceived stress and birth outcomes. When expected cell counts for categorical variables were less than five, Fisher's Exact Test was conducted.

Multivariable logistic regression was used to assess whether perceived stress during pregnancy was associated with each of the adverse birth outcomes. Early, mid- and late pregnancy perceived stress levels were examined when assessing the associations with low birth weight and SGA. Only early and mid-pregnancy perceived stress levels were included in the preterm birth analysis as a number of preterm births occurred before the late pregnancy interviews could be conducted. Models were developed with perceived stress as a continuous variable and categorized as quartiles. Age, BMI and parity were included as *a priori* confounders in regression models as they are known risk factors for preterm birth, low birth weight, and SGA. In addition, history of preterm birth was also included as an *a priori* confounder in the preterm birth analysis. Other potential confounders were included in the final model if the odds ratio between perceived stress and the given adverse birth outcome changed by more than 10% when the confounder was included in the model. As in bivariate analyses, only time varying covariates from the same pregnancy period as the stress measure were assessed as confounders. If more than 35 participants were missing values for a given confounder, a missing category was used for that confounder in analyses. A test for trend was performed to assess linearity between increasing stress level quartiles and each of the adverse birth outcomes.

A series of adjusted models were examined for each adverse birth outcome. Adjusted Model 1 included potential sociodemographic, physical, health and acculturation confounders. Adjusted Model 2 included factors in Model 1 in addition to

identified behavioral factors. These factors were included in separate analyses because of the possibility that they could be in the causal pathway by either leading to increased stress or occurring as a result of stress. Model 3 includes Model 1 factors and additionally adjusts for other psychological measures identified as confounders. Psychological measures were added to the model separately because of the possibility that they also may be in the causal pathway. Model 4 includes all identified confounders. Unadjusted analyses were also conducted examining the effect of stress on subcategories of preterm births as stress has been suggested to have an association with specific subcategories. In separate regression analyses, we examined the association between perceived stress and preterm births that were spontaneous, medically indicated, early and late.

As stress, depression and anxiety commonly co-occur, collinearity between perceived stress and anxiety and depression was assessed by examining 1) crosstabulations between perceived stress and each of the two psychosocial factors, 2) standard errors for the beta coefficients of stress, depression and anxiety when included simultaneously in the regression model, and 3) condition indices and variance inflation factor (VIF) values. Based on these analyses, it was determined that an important degree of collinearity did not occur between stress and these two psychosocial factors.

Effect modification between perceived stress and anxiety and depression was assessed to determine whether the association between perceived stress and each of the adverse birth outcomes varied depending on the level of depression and/or anxiety experienced by study participants. Interaction terms could not be used to assess effect modification due to sample size limitations and too few study participants within some

strata, which led to non-estimability when running the regression model. Therefore, stratified analyses were conducted to examine the association between stress and each of the adverse birth outcomes by level of depression (probable major depression, not probable major depression) and anxiety (high anxiety, not high anxiety). In addition, composite variables of stress and depression (low stress/not probable major depression, low stress/probable major depression, high stress/probable major depression, high stress/probable major depression) and stress and anxiety ((low stress/low anxiety, low stress/high anxiety, high stress/low anxiety, high stress/high anxiety) were each examined in regression analyses with each of the adverse birth outcomes.

We also examined whether patterns of perceived stress during pregnancy affected risk for adverse birth outcomes. Specifically, we assessed whether the following were associated with adverse birth outcomes: (1) change in perceived stress level over the course of pregnancy, and (2) greater duration of exposure to stress during pregnancy (e.g. high stress at single timepoint vs. across the entire pregnancy). Change in stress score was examined from early to mid-, mid- to late, and early to late pregnancy for low birth weight and SGA. Only early to mid-pregnancy changes in PSS score were examined when assessing the association with preterm births as a number of women that had preterm births were missing late pregnancy interviews. Duration of exposure to high stress was examined from early to mid-pregnancy for all three birth outcomes, and from mid- to late pregnancy for low birth weight and SGA.

As some studies have shown that antidepressant use may be associated with adverse birth outcomes, [76] a sensitivity analysis was conducted examining the effect of stress on each of the adverse birth outcomes in a subset of patients that 1) did not have

documented self-reported antidepressant use during pregnancy in the electronic medical record database, or 2) that were not found to have been prescribed antidepressants during pregnancy in the electronic prescription database. All analyses were conducted using SAS version 9.2 (SAS Institute Inc, Carey, NC).

Results

Study Population Characteristics

Among the 1,266 participants included in the study, the mean age was 22.8 years, with approximately 70% of women age 25 years or younger (Table 1.1). Forty-seven percent of participants were born in Puerto Rico or the Dominican Republic and 79.2% of the study population was categorized as having low levels of acculturation. Women were generally of low socioeconomic status with 58% of those that reported income having an income of less than $15,000 per year, and almost 48.8% of women reporting that they did not receive a high school diploma or GED. Fifty-one percent of participants reported living with a partner or spouse and 41.9% were nulliparous. Approximately a third of women reported smoking and 40% reported drinking alcohol in the year prior to pregnancy, with far fewer reporting these risk behaviors in early pregnancy. Eighteen percent of women were classified as having probable major depression and mean trait anxiety scores were 39.7 (standard deviation (SD)=10.4).

The overall mean perceived stress score during pregnancy was 28.3 (SD= 6.8). Mean perceived stress scores were highest in early pregnancy and decreased over the course of pregnancy, ranging from early pregnancy mean scores of 26.2 (SD=7.1) to late pregnancy mean scores of 23.3 (SD=7.8) (Table 1.2).

Among study participants, 9.3% had a preterm birth (n=118), 7.8% had an infant that was born low birth weight (n=98), and 12.5% an infant that was SGA (n=157)(Table 1.3). When examining births born preterm, 75% were spontaneous and 71% were born between 34 and 36 weeks gestation (late preterm).

Stress and Covariates

In bivariate analyses examining the associations between potential covariates and perceived stress during pregnancy, education and income were significantly associated with stress for all pregnancy periods (Table 1.4). Women with low levels of education and income experienced higher levels of perceived stress. Women that were categorized as "don't know/refused to respond" for income (approximately 25%), also had higher perceived stress levels. The only other sociodemographic factor that was associated with stress was maternal age. Women that were age 30 and over had lower levels of early pregnancy perceived stress than younger women. This trend was observed in mid- and late pregnancy, though the differences were not as pronounced and were not statistically significant.

When examining acculturation factors and perceived stress, women who were third generation Puerto Rican or Dominican-Americans had lower levels of perceived stress compared to those whose parents were born in Puerto Rico/Dominican Republic (second generation) or who were born there themselves (first generation)(Table 1.4). This association was near statistical significance in early pregnancy (p=0.09) and reached significance in mid-pregnancy (p=0.05). When examining level of acculturation, women

that had high levels of acculturation tended to have lower levels of mid- and late pregnancy perceived stress than women with low levels of acculturation.

Smoking prior to pregnancy was significantly associated with stress throughout pregnancy with women reporting pre-pregnancy smoking having higher levels of perceived stress (Table 1.4). Similarly, women that reported smoking during pregnancy had significantly greater levels of stress during the same pregnancy period when compared to women that reported not smoking. Alcohol consumption was associated with stress, though not consistently across all pregnancy periods. Women reporting that they consumed alcohol in pre-pregnancy had significantly higher levels of early pregnancy perceived stress, but not in mid- or late pregnancy. A similar positive association was found for alcohol consumption during pregnancy, but only in late pregnancy. As anticipated, state anxiety and depression were highly positively significantly associated with perceived stress at all pregnancy timepoints assessed. Trait anxiety was also associated with perceived stress throughout pregnancy.

Adverse Birth Outcomes and Covariates

In bivariate analyses, women who had preterm births or low birthweight infants were more likely to have had a history of preterm birth and have smoked in mid-pregnancy than women that had a term birth (Table 1.5). Women with low birth weight infants were also more likely to have smoked in late pregnancy. No other factors were associated with preterm birth or low birth weight.

SGA was also associated with smoking. Women that gave birth to an SGA infant were more likely to have smoked in pre-, early or late pregnancy compared to women

that did not give birth to an SGA infant. SGA was also found to be associated with pre-pregnancy parity, BMI, and education. Among women that had SGA infants, a larger proportion were identified as nulliparous and having a pre-pregnancy BMI below (less than 18.5) or within the normal range (18.5 – 25.0) as compared to women that did not have infants born SGA. In regards to education, women that had SGA infants were less likely to have completed high school or its equivalency. Finally, the only other covariate associated with SGA was late pregnancy state anxiety, with a larger proportion of women having SGA infants in the highest quartile of state anxiety when compared to women that did not have an SGA infant.

Perceived Stress and Adverse Birth Outcomes

Early pregnancy perceived stress was not associated with preterm birth in unadjusted or adjusted logistic regression analyses (Table 1.6). Mid-pregnancy perceived stress was not significantly associated with preterm birth in unadjusted analysis (Table 1.6) or multivariable analyses adjusting for identified sociodemographic/health (Table 1.6, adjusted Model 1) or behavioral confounders (Table 1.6, adjusted Model 2). However, after adjusting for sociodemographic/health and other psychological measures, a positive association was found between perceived stress and preterm birth with women experiencing higher levels of stress at greater risk for preterm birth (Table 1.6, adjusted Model 3). Women in the 2nd quartile had an odds ratio (OR) of 1.81 (95% CI= 0.80, 4.10), the 3rd quartile an OR of 2.55 (95% CI= 1.14, 5.67), and the 4th quartile an OR of 3.80 (95% CI= 1.58, 9.16; $p\text{-}_{trend}<0.01$) when compared to women in the lowest quartile. A positive association was also found for the continuous measure of perceived stress with

a 1-unit increase in the PSS associated with a 7% greater odds of preterm birth (OR=1.07, 95% CI=1.02,1.12). After further adjusting for behavioral factors, associations remained significant, though were slightly attenuated for the continuous measure of perceived stress and the highest quartile of the categorical measure (Table 1.6, Model 4).

Early pregnancy perceived stress was not found to be associated with low birth weight in unadjusted analysis (Table 1.7) or after adjusting for sociodemographic/health factors (Table 1.7, adjusted Model 1). However, after further adjusting for other psychological measures, there was found to be a significant positive association with every 1-unit increase in the PSS associated with a 7% higher risk of LBW (OR=1.07, 95% CI=1.01, 1.12). Similarly, when early pregnancy perceived stress was analyzed as a categorical variable in this adjusted model, women at higher levels of perceived stress had greater odds of low birth weight compared to women that had the lowest level of stress, though the findings were not significant (1.7, adjusted Model 3).

Greater levels of mid-pregnancy perceived stress was found to increase risk for low birth weight in both unadjusted and adjusted analyses. In unadjusted analyses, elevated risk was found for each 1-unit increase in the continuous PSS measure (OR=1.04, 95% CI=1.00, 1.08). Though risk was elevated with increasing quartiles of perceived stress in unadjusted analyses, the increased risk approached, but did not reach significance (Q4 OR=2.11, 95% CI=0.95, 4.70). However, after adjusting for sociodemographic/health factors (Table 1.7, adjusted Model 1), the increases in risk became more pronounced and statistically significant with women in the 3rd quartile experiencing 2.4 times the risk of low birth weight (OR=2.41, 95% CI=1.04, 5.55), and those in the highest quartile just over 2.5 times the risk of having a low birth weight baby

(OR=2.52, 95% CI=1.10, 5.82; p-trend=0.01) compared to women in the lowest quartile. The continuous PSS measure retained significance comparable to unadjusted values. Models did not adjust for behavioral or psychological factors as none were identified as confounders. Late pregnancy perceived stress was not found to be associated with low birth weight in unadjusted analysis or adjusted analyses.

Perceived stress during pregnancy was not found to be associated with SGA in adjusted or unadjusted analyses (table 1.8). Neither the continuous nor categorical perceived stress measure was associated with increased risk.

Antidepressant use is a possible confounder of the association between perceived stress and adverse birth outcomes. Thirty-one women (2.4% of participants) were identified as likely having used antidepressants based on information gathered from the medical record and prescription databases. In sensitivity analyses that did not include these women, findings remained the same with elevated levels of mid-pregnancy perceived stress associated with both preterm birth in adjusted analysis, and low birth weight in both unadjusted and adjusted analyses (Table 1.9). Of note, the estimates of effect were more pronounced after removing women with likely pregnancy antidepressant use than those in the comparable unadjusted and adjusted full analyses that included all participants.

Stress, Anxiety, Depression and Adverse Birth Outcomes

Analyses were conducted to determine whether the effect of stress on risk for adverse birth outcomes varied by anxiety and depression level. In unadjusted stratified logistic regression analysis that examined perceived stress as a continuous measure, it

was found that increased levels of mid-pregnancy perceived stress increased risk for preterm birth and low birth weight among women that did not have probable major depression (OR_{PTB}=1.05, 95% CI=1.01, 1.10; $OR_{LBW=}$1.05, 95% CI=1.00, 1.10)(Table 1.10). Similar increased risk due to greater levels of mid-pregnancy perceived stress was observed for preterm birth among women who did not have high levels of anxiety (OR=1.05, 95% CI=1.00, 1.10). The effect estimate was also elevated among women that had probable major depression and among those that had high levels of anxiety, though to a lesser extent and the findings were not statistically significant; however, power was limited to detect an effect due to smaller sample sizes in these strata. Perceived stress in early and late pregnancy was not significantly associated with preterm birth or low birth weight. No associations were found between perceived stress during pregnancy and SGA.

Composite variables of stress and depression and stress and anxiety were examined in unadjusted and adjusted analyses to better understand potential interactive or synergistic effects. Women who had both a high level of perceived stress and a high level of state anxiety in late pregnancy were at increased risk for having an infant born SGA when compared to women that had low levels of both stress and anxiety in unadjusted (OR=1.98, 95% CI=1.13, 3.49) and adjusted analyses (OR=2.08, 95% CI=1.16, 3.72)(Table 1.11). No other associations were observed between the composite variables and birth outcomes.

Patterns of Perceived Stress and Adverse Birth Outcomes

When examining the effects of patterns of perceived stress during pregnancy on preterm birth, low birth weight and SGA, change in PSS score from early to mid-pregnancy was not associated with any of the adverse birth outcomes. Upon examination of change in PSS scores from early to late pregnancy, it was found that for each unit increase in the PSS, there was a 5% increase in odds of SGA in adjusted analyses that included control for stress in early pregnancy (OR=1.05, 95% CI=1.00, 1.09). This association was not observed in unadjusted analyses or analyses that only adjusted for sociodemographic/health factors. No other associations were found between the continuous change measure of the PSS at any timepoint and preterm birth, low birth weight, or SGA. In addition, when change scores were grouped as decrease vs. no change/increase no associations were found with any of the adverse birth outcomes (Table 1.12).

When evaluating duration of exposure to high stress during pregnancy as a potential risk factor for preterm birth, low birthweight and SGA, exposure to high levels of perceived stress in one or two time periods was not found to increase risk for any of the adverse birth outcomes when compared to women that did not experience high levels of stress during pregnancy (Table 1.12).

Perceived Stress and Type of Preterm Birth

In unadjusted analyses assessing the association between perceived stress and types of preterm birth, no association was found between level of perceived stress and spontaneous or medically indicated preterm births (Table 1.13). Similarly, no association

was found when examining the relationship between stress and types of spontaneous preterm birth (preterm labor, PPROM). When examining whether perceived stress is associated with preterm births categorized by gestational age, no associations were found with either early or late preterm births (Table 1.13). However, power was limited in these analyses due to small sample size.

Discussion

In one of few prospective cohort studies examining whether stress during pregnancy is associated with preterm birth, low birth weight, and SGA in a Hispanic population, we found that higher levels of perceived stress in mid-pregnancy increased risk for low birth weight in adjusted analyses. A similar association was found between mid-pregnancy stress levels and preterm birth, in adjusted analyses that included the other psychological measures of depression and anxiety. Stress in early pregnancy was found to be associated with low birth weight in adjusted analysis that included other psychological measures, but only when stress was assessed as a continuous measure. Stress was not associated with preterm birth or low birth weight at any other time point, or with SGA at any time during pregnancy. However, women that experienced high levels of both stress and anxiety in late pregnancy had a higher risk of giving birth to an SGA infant when compared to women that did not have high levels of either. In addition, increase in PSS score from early to late pregnancy was found to increase risk for SGA. Duration of exposure to stress during pregnancy was not associated with any of the adverse birth outcomes examined.

Our findings that greater levels of stress increase risk for preterm birth and low birth weight are similar to those of several other studies,[21, 24, 27, 35, 53, 77, 78] though some studies have not found this association.[28, 31, 33, 41, 49, 52, 79] In one of the only other studies to examine the association between stress and preterm birth or low birth weight in a Hispanic population, Ruiz et. al did not find that a greater level of perceived stress was associated with gestational age.[79] This study consisted of a predominantly Mexican-American study population. Among the other few studies that included a predominantly Hispanic population, most found that stress increased risk for preterm birth, or decreased gestational age at birth, as well as lower birth weight.[35, 77, 80] Our findings that stress was not associated with SGA when stress was examined as an independent predictor is consistent with the majority of studies examining this association.[27, 49, 51-54, 57, 58, 60, 81]

Difference in exposure to chronic stress is one of several factors that may account for variation in study findings. The Hispanic women included in this study were predominantly of low SES and have likely experienced high levels of chronic stress due to lack of resources and other challenges. This is reflected in the high mean PSS scores, with a mean score in early pregnancy (mean=26.2, SD=7.1) higher than that found for women (mean=20.2, SD=7.8) or Hispanics (mean=21.3, SD=7.8) in a U.S. probability sample.[23] Generally, when stress has been assessed with the PSS, fewer studies have shown a positive association between stress at a single timepoint and preterm birth or low birth weight. It is possible that the discrepancy in findings from studies examining the association between perceived stress and preterm birth and low birth weight are due to potential complexities related to the effect of chronic stress on physiological mechanisms as discussed in the physiologic mechanism section below.

Patterns of Stress

Only two other studies have examined the effects of patterns of stress on adverse birth outcomes with both focusing on preterm birth/gestational age. As discussed previously, increases in stress over the course of pregnancy are theorized to indicate a susceptibility to stress, as research suggests that both the physiologic stress response and the appraisal of experiences as stressful diminish as pregnancy progresses.[22, 26] Glynn et al. found that an increase in perceived stress from mid- to late pregnancy as a dichotomous measure was associated with an increased risk of preterm birth, though change in stress as a continuous measure was not associated with preterm birth.[22] Ruiz et al. found an inverse linear association between perceived stress from mid- to late pregnancy, as a continuous measure, and length of gestation.[24] Interestingly, neither study found an association between perceived stress and length of gestation or preterm birth at either timepoint. When examining patterns of stress and preterm birth, we were only able to examine change in stress from early to mid- pregnancy. We did not find an association between change in stress during this timeframe and preterm birth. However, we did find that increases in perceived stress from early to late pregnancy were associated with increased risk for SGA. This is the first study to our knowledge to examine the effect of pattern of perceived stress during pregnancy on SGA and low birth. We did not find an association between pattern of perceived stress and low birth weight.

No other studies have examined the effect of duration of exposure to stress and adverse birth outcomes. This may be particularly relevant to low birth weight and SGA, as chronic exposure to glucocorticoids and catecholamines associated with the stress

response are believed to be associated with growth restriction and prolonged growth restriction may lead to the clinical outcomes of low birthweight and SGA. To our knowledge, this is the first study to examine duration of exposure to high levels of stress during pregnancy and low birth weight or SGA. We did not find that a greater duration of exposure increased risk for low birth weight or SGA.

Stress, Anxiety and Depression – the Role of other Psychological Factors

Few studies have examined how stress may interact with other psychological factors, particularly depression and anxiety, to affect risk for adverse birth outcomes, and those that have been conducted have focused on preterm birth.[38, 82] Our study found that women that had high levels of stress and anxiety in late pregnancy were at increased risk for an infant born SGA. It is possible that the combination of these factors may increase risk for SGA, or that women with high levels of stress or anxiety are at increased risk for SGA when compared to women that do not have high levels of stress or anxiety. Conversely, it is also possible that these women learned that their fetus was small-for-gestational age during pregnancy, which led to high levels of stress and anxiety in late pregnancy. More research is needed to better understand how high levels of stress and anxiety may affect fetal growth.

The majority of studies have accounted for depression and anxiety by adjusting for these factors in analyses to gain an understanding of the role of stress as an independent risk factor since these psychological factors often co-occur.[28, 30, 34, 43, 44, 83, 84] Our study found that elevated levels of mid-pregnancy stress increased risk for low birth weight in adjusted analyses that included depression and anxiety. However, we found

that early pregnancy stress only increased risk for low birth weight when adjusted analyses included trait anxiety, which was the only psychological factor found to be a confounder. Similarly, when examining preterm birth, we found that though women with higher levels of mid-pregnancy stress had greater odds of preterm birth in adjusted analyses that did not include anxiety and depression, the risk did not become significant until after these psychological factors were included as confounders in the adjusted model. When interpreting these findings, one must consider the interrelationship between stress, anxiety, and depression. Both constructs underlying some psychological factors and the instruments used to measure them have a fair amount of overlap, which can be problematic when attempting to tease out independent effects in health research. [85] Conceptually, perceived stress, anxiety and depression are related, as stress is believed to be a precipitating factor for anxiety and depression disorders in some cases.[86, 87] Similarly, there are overlaps between the PSS, the EPDS and the STAI. For example, all three instruments have questions related to control and coping. Our findings suggest that aspects of perceived stress not shared with depression and anxiety may increase risk for preterm birth.

Physiologic Mechanism between Stress and Risk for Adverse Birth Outcomes

Several mechanisms have been proposed to explain how stress may increase risk for adverse birth outcomes, primarily focusing on the physiologic stress response and on behavioral risk factors associated with stress (e.g. smoking). We found that elevated levels of perceived stress in mid-pregnancy increased risk for preterm birth in analyses that included adjustment for traditional risk factors, other psychological measures, and

smoking and alcohol consumption. Smoking and alcohol consumption were not included in adjusted analyses examining the effect of stress on low birth weight as they were not found to be confounders in our analyses, though in subanalyses, the effect remained when these two behavioral risk factors were included in the model (results not shown). These findings suggest that other mechanisms may be responsible for increased risk due to stress, including the physiologic stress mechanisms (e.g. CRH, norepinephrine, cortisol) discussed previously.

As discussed earlier, differences in levels of stress hormones and HPA axis function during pregnancy have been found to vary by race/ethnicity.[6, 7, 15-17] It is not clear if these differences are due to exposure to chronic stress experienced by some racial/ethnic groups or other factors that may lead to these differences. Exposure to chronic stress is believed to lead to different effects than acute stress. Animal research suggests that exposure to chronic stress leads to a dysregulation of the HPA axis and a blunted physiologic stress response over time.[88] However, a recent review by Herman concludes that though there is a habituation to the chronic stressors, the research suggests that there is also an increased sensitivity and reactivity to new stressors.[89] In addition, findings from some studies suggests that stress hormones may have a different effect among those that are chronically stressed such that lower levels of glucocorticoids may have more pronounced effects on body systems.

These findings support Kramer's theory that chronic stress may lead to lower levels of CRH during pregnancy found in some racial/ethnic groups, but that risk for preterm birth associated with increases in CRH is greater among women exposed to chronic stress.[18] However, as some studies have found that racial/ethnic differences in

stress hormone levels during pregnancy have persisted after adjustment for factors that are likely contributors to exposure to chronic stress, such as indicators of socioeconomic status, more research is needed to understand the causes of these differences and how they affect risk for adverse birth outcomes among these at-risk populations. We found that elevated levels of stress in mid-pregnancy increased risk for preterm birth and low birth weight in a population of Hispanic women. This has not been consistently found in other studies, but this may be due to potential racial/ethnic differences in study populations and/or differences in exposure to chronic stress.

Strengths and Limitations

Our study is one of few studies to examine the association between stress and adverse birth outcomes in a Hispanic population. In addition, it is one of few studies to examine stress at multiple time points during pregnancy and the effect of patterns of exposure to stress during pregnancy on preterm birth. It is the only study to examine the effect of patterns of exposure to stress on low birth weight and SGA. Our study included adjustment for a number of confounders, which is lacking in some studies. Also, we used a measure of stress, perceived stress, that takes into account the stress appraisal process. We also explored how stress may act in synergy with depression and anxiety to increase risk for adverse birth outcomes, and the independent effect of stress when taking into account these psychological factors.

Our study is subject to several potential limitations. Nondifferential misclassification of perceived stress may have occurred. Though the PSS has been demonstrated to have adequate reliability (Cronbach's alpha=0.75-0.81, rest-retest

reliability=0.55-0.85), reliability measures were below the "good" or "excellent" range indicating the potential for misclassification. In addition, there is likely individual variability in one's willingness to answer affirmative to PSS questions stating that they feel "out of control" or "unable to cope". Also, though the Spanish version of the PSS has demonstrated good reliability in a European Spanish population, the instrument has not been validated in a Spanish-speaking population in the United States, particularly a Puerto Rican population. Previous research has shown that reliability of the scale may vary across Spanish-speaking populations of differing descent, likely due to differences in interpreting the questions.[90] Thus, it is possible that the instrument's reliability is lower in a Puerto Rican population. Nondifferential misclassficiation of stress would have biased our results towards the null. Though it is likely that this occurred to some degree, we expect that it did not significantly affect our results.

It is possible that misclassification of preterm birth occurred as gestational age is determined through the "best clinical estimate," which most frequently used ultrasound and LMP. As ultrasounds are evaluated based on average growth trajectories, and these averages may not reflect individual growth patterns, the obstetrician identified gestational age at birth may not reflect the "true" gestational age of the infant. LMP provides a more inexact estimate of gestational age as it assumes an average 14 days between LMP and conception that does not reflect the wide-range of individual variability. Variability in both these estimates would lead to nondifferential misclassification of preterm births, which would bias the results towards the null. However, we do not expect large differences between the "true" and obstetrician identified gestational age.

This potential misclassification of gestational age would also occur when identifying SGA infants, as case status is determined by gestational age information in addition to birth weight. Similarly, we would expect nondifferential misclassification to occur when determining SGA. SGA would be subject to an additional potential source of nondifferential misclassification as the weight for gestational age cut-points used to identify SGA infants are based on a Hispanic population of varying descent,[74] and studies have found that average birth weights may vary among Hispanics based on country of descent.[3] Another possible source of misclassification for SGA is the potential variation in birth weight measurement as the scales used to measure newborns likely have some measurement variability, though we anticipate this to be minimal as they are regularly calibrated. This would also be a potential source of misclassification for low birth weight. Nondifferential misclassification of any of the adverse birth outcomes would bias the results to the null.

Selection bias could have occurred as we did not have complete stress data on participants over the course of pregnancy and it is possible that woman with high stress levels may have dropped out or did not participate in all of the interviews because of their high stress. When comparing study participants with mid-pregnancy stress data to those without, we found that trait anxiety was higher among participants that did not have mid-pregnancy stress data, though levels did not quite reach statistical significance (Trait Anxiety 4th Quartile: with mid-pregnancy PSS data=21.5%; without mid-pregnancy PSS data=25.8%). Similarly, the prevalence of likely major depression in early pregnancy was slightly higher among women missing mid-pregnancy stress data (18.6%) when comparing to women with mid-pregnancy data (17.5%). As trait anxiety and major

depression were positively associated with stress in our population, this suggests that participants that did not have mid- and late pregnancy stress data may have had higher stress levels. In addition, low birth weight rates were higher among women missing mid-pregnancy stress data when compared to those with mid-pregnancy data (8.8% vs. 7.2%). Preterm birth rates did not vary substantially between women with (9.2%) and without (9.5%) mid-pregnancy stress data. Thus, it is possible that women with high mid-pregnancy stress levels that gave birth to low birth weight babies were more likely to have incomplete mid-pregnancy data, which could have lead to a bias to the null for the association between mid-pregnancy stress and low birth weight. If stress were associated with preterm birth, low birth weight or SGA in late pregnancy, then these results would also be biased towards the null.

As this is a prospective study, information bias would occur if adverse birth outcome status was ascertained differentially based on stress level. This is unlikely to have occurred as information on adverse birth outcome status was obtained through medical record abstraction by an abstractor blinded to the stress level of the participant. In addition, the study obstetrician that verified cases of preterm birth was also blinded to the stress level of the participants during pregnancy.

We adjusted for a number of important confounders in our analyses. One important potential confounder that we did not have complete information on was anti-depressant use. Stress is positively associated with depression,[25] and subsequently anti-depressant use. Though results have been conflicting overall, some studies have shown that the use of some anti-depressants during pregnancy may be associated with increased

risk of preterm birth, low birth weight and SGA,[76] thus indicating the potential for positive confounding. Using information from electronic medical records and the hospital prescription database, we conducted a sensitivity analysis to determine if the relationship between stress and each of the adverse birth outcomes is different among participants that were not prescribed antidepressants during pregnancy. We found that the association between perceived stress and preterm birth and low birth weight persisted when only including those woman that did not report antidepressant use or that were not prescribed antidepressants. However, it is unlikely that all woman that took antidepressants were identified through this method as only 31 woman were identified. In addition, the anti-depressant use information was subject to potential misclassification as it is possible that some women prescribed antidepressants did not take them. Also, women that were prescribed anti-depressants by a health provider outside of Baystate Health System were not included as the database only included women prescribed medication by a Baystate provider. However, as we found that the effect estimate of the association between perceived stress and low birth weight became more pronounced with the exclusion of the women prescribed or self-reporting anti-depressant use, we do not anticipate that confounding accounted for our results.

Another set of potential confounders that we did not adjust for are maternal pregnancy complications, such as gestational diabetes mellitus (GDM), gestational hypertension and pre-eclampsia. Generally, these conditions may increase risk for adverse birth outcomes, though in the case of GDM, risk for growth restriction may decrease as GDM may lead to macrosomia. In addition, it is possible that discovery of these conditions may increase stress for the mother in mid- to late pregnancy as they are

typically diagnosed or manifest during this timeframe, which creates the potential for positive confounding. Though data was available for these conditions, we were unable to adjust for them in multivariable logistic regression analysis due to the rarity of occurrence leading to small sample size within some strata. Therefore, we conducted a sensitivity analysis excluding participants with GDM, gestational hypertension or pre-eclampsia. We found that that association between mid-pregnancy stress score (continuous) and low birth weight persisted after excluding these participants.

The results of these studies may be generalizable to pregnant Hispanic women and also women that have experienced chronic stress. Hypothesized mechanisms explaining the relationship between stress and the adverse birth outcomes of interest primarily involve CRH and cortisol and studies suggest that levels of these hormones may vary during pregnancy.[6, 16] In addition, it has been found that the effect of cumulative stress on cortisol levels during pregnancy may vary by ethnic background.[7] If these hormone levels are inherently different for Hispanic women during pregnancy and the effect of stress on these hormone levels varies by race/ethnicity, it is possible that the relationship between stress and preterm birth, low birth weight, and SGA would be different for women from other racial/ethnic backgrounds. However, it has also been suggested that these racial/ethnic differences may have occurred as a result of chronic stress.[18] If this is the case, then the results would be generalizable to women that have experienced chronic stress.

Conclusion

Few studies have examined the association between stress and preterm birth, low birth weight, and small-for-gestational age in a Hispanic population. Those that have been conducted focused primarily on a Mexican population and were limited by small sample size. Given the differences in stress hormone levels and HPA-axis function during pregnancy observed in some racial/ethnic groups, it is important to examine the effect of stress within Puerto Rican women and other high risk groups that experience disproportionately high rates of these adverse birth outcomes. Many of the groups experiencing these disparities are subject to numerous stressors during pregnancy and over the course of the lifetime. We are only beginning to understand the complexities of the physiologic stress processes and how these processes may affect health and contribute to disparities, including those related to adverse birth outcomes. Research suggests that exposure to stressors over the lifecourse, including chronic stress and exposure to stress during susceptible periods of exposure such as those in utero, may affect both physiologic stress response to stressors later in life, including during pregnancy. These complexities likely contribute to the inconsistent findings in the literature when examining the role of stress during pregnancy and adverse birth outcomes. Our study found that in a high risk population of Puerto Rican woman that has experienced chronic stress, perceived stress in mid-pregnancy and increases in perceived stress over the course of pregnancy increased risk for some adverse birth outcomes. More research is needed to better understand the stress processes that contribute to these increased risks.

Table 1.1 Participant characteristics: Proyecto Buena Salud, 2006-2011 (n=1266)

Categorical Measures	n	%
Maternal Age		
16-19	396	31.3
20-24	498	39.3
25-29	223	17.6
≥30	149	11.8
missing		
Pre-Pregnancy BMI		
less than 18.5	78	6.2
18.5-<25.0	604	48.1
25.0-<30.0	292	23.3
30 or greater	281	22.4
missing	11	
Education		
Less than high school	582	48.8
High school graduate or GED	386	32.4
Post high school	224	18.8
missing	74	
Income		
less than $15,000	357	30.2
$15,000-$30,000	182	15.4
$30,000 or greater	75	6.4
Don't Know/Refused	567	48.0
missing	85	
Parity		
0 live births	529	41.9
1 live birth	381	30.2
2 or more live births	353	28.0
missing	3	
Acculturation		
Low	897	79.2
High	235	20.8
missing	134	
Generation in U.S.		
Born in PR/DR	576	47.0
Parent born in PR/DR	580	47.4
Grandparent born in PR/DR	69	5.6
missing	41	
Live with partner/spouse		
no	574	48.7
yes	604	51.3
missing	88	
Smoking (pre-pregnancy)		
no	801	67.1
yes	392	32.9
missing	73	

Table 1.1 Participant characteristics: Proyecto Buena Salud, 2006-2011 (n=1266)(continued)

Categorical Measures		**n**	**%**
Alcohol (pre-pregnancy)			
	no	718	60.2
	yes	475	39.8
	missing	73	
Smoking (early pregnancy)			
	no	718	85.9
	yes	118	14.1
	missing	430	
Alcohol (early pregnancy)			
	no	818	97.4
	yes	22	2.6
	missing	426	
Probable Major Depression (early pregnancy)			
	no	687	82.0
	yes	151	18.0
	missing	428	
Continuous Measure		**Mean**	**SD**
Trait Anxiety		39.7	10.4

Table 1.2 Distribution of perceived stress (PSS-14 scores) in the study population: Proyecto Buena Salud, 2006-2011 (n=1266)

Stress- Continuous	**Mean**	**SD**
Overall Pregnancy (n=1266)	24.8	6.8
Early Pregnancy (n=862)	26.2	7.1
Mid-Pregnancy (n=794)	25.2	7.3
Late Pregnancy (n=766)	23.3	7.8

				PSS Score		
Stress Quartiles		**n**	**%**	**Mean**	**SD**	**IQR**
Early Pregnancy						
	Quartile 1	268	31.1	18.2	3.6	5.0
	Quartile 2	190	22.0	24.5	1.2	3.0
	Quartile 3	207	24.0	28.8	1.4	2.0
	Quartile 4	197	22.9	35.7	3.7	4.0
Mid Pregnancy						
	Quartile 1	214	27.0	16.1	3.7	5.0
	Quartile 2	195	24.6	23.1	1.4	2.0
	Quartile 3	195	24.6	27.9	1.4	2.0
	Quartile 4	190	23.9	34.6	3.4	4.0
Late Pregnancy						
	Quartile 1	196	25.6	13.8	4.0	5.0
	Quartile 2	200	26.1	20.9	1.4	2.0
	Quartile 3	181	23.6	26.0	1.4	2.0
	Quartile 4	189	24.7	33.3	4.3	5.0

Table 1.3 Distribution of birth outcomes in the study population: Proyecto Buena Salud, 2006-2011 (n=1266)

		n	%
Preterm Birth* - Total (n=1266)			
	Yes	118	9.3
	No	1148	90.7
Low Birth Weight (n=1252)**			
	Yes	98	7.8
	No	1154	92.2
Small for Gestational Age* (n=1252)**			
	Yes	157	12.5
	No	1095	87.5
Type of Preterm Birth			
Preterm Birth Precipitating Event			
Medically Indicated			
	Yes	28	2.4
	No	1148	97.6
Spontaneous			
	Yes	89	7.2
	No	1148	92.8
PPROM			
	Yes	33	2.8
	No	1148	97.2
Pre-term labor			
	Yes	56	4.7
	No	1148	95.3
Preterm Birth by Gestational Age			
Early preterm (<34 weeks)			
	Yes	34	2.9
	No	1148	97.1
Late Preterm (34-36 weeks)			
	Yes	84	6.8
	No	1148	93.2

*gestational age <37 weeks
**less than 2,500 grams
*** less than 10th percentile of weight for gestational age

Table 1.4 Distribution of covariates by stress quartiles in the study population: Proyecto Buena Salud, 2006-2011

	PSS Scores (continuous)								
	Early Pregnancy			Mid-Pregnancy			Late Pregnancy		
	mean	SD	p-value*	mean	SD	p-value*	mean	SD	p-value*
Maternal Age									
16-19	26.17	7.03	<0.01	25.79	6.95	0.19	23.93	7.30	0.16
20-24	26.90	6.70		25.24	7.29		23.47	7.80	
25-29	26.35	7.14		24.66	7.47		22.90	8.03	
≥30	23.39	8.18		24.02	8.10		21.76	8.47	
Pre-Pregnancy BMI									
less than 18.5	26.14	6.51	0.09	25.18	6.17	0.37	23.51	8.35	0.93
18.5-<25.0	26.63	6.85		25.49	7.25		23.51	7.59	
25.0-<30.0	25.06	7.66		24.33	7.33		23.05	7.56	
30 or greater	26.23	7.29		25.34	7.82		23.27	8.26	
Education									
Less than high school	26.97	7.20	<0.01	25.54	7.29	0.02	24.22	7.84	<0.01
High school graduate or GED	25.88	7.02		23.27	7.21		23.19	7.66	
Post high school	24.46	6.94		23.45	7.11		21.89	7.13	
Income									
less than $15,000	26.75	7.39	<0.01	26.56	7.40	<0.01	24.33	8.06	0.01
$15,000-$30,000	25.27	6.84		23.38	6.70		21.89	6.89	
$30,000 or greater	22.97	6.87		21.19	7.43		21.45	7.61	
Don't Know/Refused	26.50	7.01		25.07	7.10		23.75	7.58	
Parity									
0 live births	26.20	6.84	0.95	25.26	7.21	0.90	22.95	7.47	0.53
1 live birth	26.02	7.07		24.98	7.36		23.50	7.47	
2 or more live births	26.16	7.24		25.20	7.54		23.67	8.55	
History of Preterm Delivery									
no	26.18	7.14	0.73	25.13	7.29	0.69	23.22	7.81	0.12
yes	25.89	7.17		25.46	7.55		24.86	7.67	
History of IUGR									
no	26.04	7.10	0.67	25.09	7.30	0.59	23.39	7.79	0.94
yes	24.50	8.06		29.00	.		23.00	7.07	
Acculturation									
Low	26.11	7.02	0.84	25.35	7.10	0.06	23.76	7.50	0.06
High	25.99	7.54		24.04	7.79		22.47	7.96	
Generation in U.S.									
Born in PR/DR	25.89	7.03	0.09	24.71	7.39	0.05	23.14	7.62	0.88
Parent born in PR/DR	26.67	7.48		25.76	7.36		23.40	8.12	
Grandparent born in PR/DR	24.53	5.32		23.59	6.53		22.96	5.57	
Live with partner/spouse									
no	26.38	7.36	0.38	25.43	7.42	0.22	23.95	7.74	0.12
yes	25.95	6.95		24.77	7.16		23.08	7.59	
Trait Anxiety									
1st Q	19.88	5.69	<0.01	19.36	6.39	<0.01	18.63	7.05	<0.01
2nd Q	23.95	4.89		23.59	5.61		22.08	6.06	
3rd Q	27.50	4.59		26.96	5.50		25.38	5.78	
4th Q	33.00	5.62		30.50	6.26		29.33	7.25	
Pre-Pregnancy									
Smoking									
no	25.40	6.81	<0.01	24.53	7.22	<0.01	22.81	7.50	<0.01
yes	27.55	7.60		26.34	7.21		24.59	8.06	
Alcohol									
no	25.57	7.11	<0.01	24.81	7.64	0.17	23.10	7.75	0.19
yes	26.97	7.10		25.56	6.63		23.86	7.63	

Table 1.4 Distribution of covariates by stress quartiles in the study population: Proyecto Buena Salud, 2006-2011 (continued)

	PSS Scores (continuous)								
	Early Pregnancy			Mid-Pregnancy			Late Pregnancy		
	mean	SD	p-value*	mean	SD	p-value*	mean	SD	p-value*
Early Pregnancy									
Smoking									
no	25.10	7.07	<0.01	n/a	n/a		n/a	n/a	
yes	28.64	7.37							
Alcohol									
no	26.10	7.19	0.33	n/a	n/a		n/a	n/a	
yes	27.62	6.88							
Probable Major Depression									
no	24.60	6.52	<0.01	n/a	n/a		n/a	n/a	
yes	32.94	5.73							
Mid-Pregnancy									
Smoking									
no	n/a	n/a		24.69	7.18	<0.01	n/a	n/a	
yes				28.28	7.57				
Alcohol									
no	n/a	n/a		25.11	7.34	0.21	n/a	n/a	
yes				28.38	5.29				
Probable Major Depression									
no	n/a	n/a		23.38	6.56	<0.01	n/a	n/a	
yes				33.00	5.12				
State Anxiety									
1st Q	n/a	n/a		19.67	6.83	<0.01	n/a	n/a	
2nd Q				23.18	5.60				
3rd Q				26.00	5.90				
4th Q				31.29	5.54				
Late Pregnancy									
Smoking									
no	n/a	n/a		n/a	n/a		23.00	7.65	<0.01
yes							26.14	8.41	
Alcohol									
no	n/a	n/a		n/a	n/a		23.22	7.70	<0.01
yes							31.70	10.30	
Depression									
no	n/a	n/a		n/a	n/a		21.91	7.06	<0.01
yes							32.72	5.64	
State Anxiety									
1st Q	n/a	n/a		n/a	n/a		17.78	6.58	<0.01
2nd Q							21.17	6.06	
3rd Q							24.70	6.15	
4th Q							30.34	6.50	

*T-test or ANOVA

Table 1.5 Distribution of covariates by birth outcomes in the study population: Proyecto Buena Salud, 2006-2011

	Preterm Birth(n=1266)					Low Birth Weight (n=1252)					Small for Gestational Age (n=1252)				
	No		Yes			No		Yes			No		Yes		
	n	%	n	%	p-value*	n	%	n	%	p-value*	n	%	n	%	p-value*
Maternal Age															
16-19	355	30.9	41	34.8	0.38	355	30.8	35	35.7	0.53	336	30.7	54	34.4	0.33
20-24	460	40.1	38	32.2		459	39.8	33	33.7		426	38.9	66	42.0	
25-29	201	17.5	22	18.6		206	17.9	16	16.3		198	18.1	24	15.3	
>=30	132	11.5	17	14.4		134	11.6	14	14.3		135	12.3	13	8.3	
Pre-Pregnancy BMI															
less than 18.5	69	6.1	9	7.8	0.37	68	5.9	8	8.3	0.12	60	5.5	16	10.3	0.05
18.5-<25.0	551	48.4	53	45.7		542	47.3	55	56.7		517	47.6	80	51.3	
25.0-<30.0	259	22.7	33	28.5		270	23.6	20	20.6		258	23.8	32	20.5	
30 or greater	260	22.8	21	18.1		265	23.1	14	14.4		251	23.1	28	18.0	
Education															
Less than high school	528	48.6	54	50.9	0.43	529	48.5	45	51.1	0.11	487	47.1	87	60.0	0.01
High school graduate or GED	349	32.1	37	34.9		350	32.1	33	37.5		347	33.6	36	24.8	
Post high school	209	19.2	15	14.2		212	19.4	10	11.4		200	19.3	22	15.2	
Income															
less than $15,000	330	30.7	27	25.5	0.62	332	30.7	22	25.3	0.27	309	30.2	45	31.1	0.42
$15,000-$30,000	166	15.4	16	15.1		168	15.5	12	13.8		160	15.6	20	13.9	
$30,000 or greater	69	6.4	6	5.7		71	6.6	3	3.5		69	6.7	5	3.5	
Don't Know/Refused	510	47.4	57	53.8		510	47.2	50	57.5		486	47.5	74	51.4	
Parity															
0 live births	477	41.7	52	44.1	0.49	474	41.2	47	48.0	0.42	437	40.0	84	53.5	0.01
1 live birth	351	30.7	30	25.4		353	30.7	26	26.5		341	31.2	38	24.2	
2 or more live births	317	27.7	36	30.5		324	28.2	25	25.5		314	28.8	35	22.3	
History of Preterm Delivery															
no	1032	91.6	90	77.6	<0.0001	1032	91.2	78	80.0	<0.01	975	90.5	135	88.2	0.37
yes	95	8.4	26	22.4		100	8.8	20	20.4		102	9.5	18	11.8	
History of IUGR															
no	n/a	n/a	n/a	n/a	n/a	1096	99.7	94	99.0	0.29**	1041	99.7	149	99.3	0.42**
yes	n/a	n/a	n/a	n/a	n/a	3	0.3	1	1.0		3	0.3	1	0.7	
Acculturation															
Low	817	78.7	80	85.1	0.14	824	79.0	64	82.1	0.52	779	79.3	109	79.0	0.94
High	221	21.3	14	14.9		219	21.0	14	18.0		204	20.8	29	21.0	
Generation in U.S.															
Born in PR/DR	517	46.5	59	52.2	0.51	523	46.7	46	48.4	0.30	500	47.1	69	45.1	0.69
Parent born in PR/DR	531	47.8	49	43.4		530	47.4	47	49.5		500	47.1	77	50.3	
Grandparent born in PR/DR	64	5.8	5	4.4		66	5.9	2	2.1		61	5.8	7	4.6	
Live with partner/spouse															
no	526	49.0	48	45.7	0.52	525	48.7	44	50.6	0.73	498	48.7	71	49.3	0.90
yes	547	51.0	57	54.3		554	51.3	43	49.4		524	51.3	73	50.7	
Trait Anxiety															
1st Q	295	27.7	31	30.7	0.48	298	27.8	24	29.3	0.73	283	27.9	39	27.7	0.42
2nd Q	257	24.1	26	25.7		259	24.3	20	24.4		245	24.2	34	24.1	
3rd Q	249	23.4	26	25.7		250	23.3	22	26.8		245	24.2	27	19.2	
4th Q	264	24.8	18	17.8		265	24.7	16	19.5		240	23.7	41	29.1	
Pre-Pregnancy															
Smoking															
no	735	67.6	66	62.3	0.27	738	67.5	53	61.6	0.27	708	68.3	83	57.6	0.01
yes	352	32.4	40	37.7		356	32.5	33	38.4		328	31.7	61	42.4	
Alcohol															
no	657	60.3	61	58.7	0.74	658	60.1	51	60.0	0.99	626	60.4	83	57.6	0.52
yes	432	39.7	43	41.4		437	39.9	34	40.0		410	39.6	61	42.4	
Early Pregnancy															
Smoking															
no	648	86.4	70	81.4	0.21	658	86.0	52	83.9	0.64	638	87.2	72	75.6	<0.01
yes	102	13.6	16	18.6		107	14.0	10	16.1		94	12.8	23	24.2	
Alcohol															
no	736	97.6	82	95.4	0.27**	749	97.4	60	96.8	0.68**	715	97.2	94	99.0	0.50**
yes	18	2.4	4	4.7		20	2.6	2	3.2		21	2.9	1	1.1	
Probable Major Depression															
no	612	81.4	75	87.2	0.18	627	81.8	53	85.5	0.46	606	82.7	72	77.4	0.21
yes	140	18.6	11	12.8		140	18.2	9	14.5		127	17.3	21	22.6	
Mid-Pregnancy															
Smoking															
no	621	88.5	52	76.5	<0.01	626	88.4	42	76.4	<0.01	591	88.0	77	84.6	0.37
yes	81	11.5	16	23.5		82	11.6	13	23.6		81	12.1	14	15.4	

Table 1.5 Distribution of covariates by birth outcomes in the study population: Proyecto Buena Salud, 2006-2011 (continued)

	Preterm Birth(n=1266)					Low Birth Weight (n=1252)					Small for Gestational Age (n=1252)				
	No		Yes			No		Yes			No		Yes		
	n	%	n	%	p-value*	n	%	n	%	p-value*	n	%	n	%	p-value*
Alcohol															
no #	690	99.0	67	98.5	0.53**	695	98.9	55	100.0	1.00**	659	98.8	91	100.0	0.61**
yes 7	7	1.0	1	1.5		8	1.1	0	0.0		8	1.2	0	0.0	
Probable Major Depression															
no #	573	81.7	57	83.8	0.67	581	82.2	43	78.2	0.46	554	82.6	68	74.7	0.07
yes #	128	18.3	11	16.2		126	17.8	12	21.8		117	17.4	23	25.3	
State Anxiety															
1st Q #	160	29.5	16	26.2	0.92	163	29.3	11	26.8	0.98	151	28.5	23	33.8	0.77
2nd Q #	111	20.4	14	23.0		114	20.5	8	19.5		109	20.6	13	19.1	
3rd Q #	140	25.8	17	27.9		145	26.0	11	26.8		141	26.6	15	22.1	
4th Q #	132	24.3	14	23.0		135	24.2	11	26.8		129	24.3	15	25.0	
Late Pregnancy															
Smoking															
no #	636	89.0	41	87.2	0.72	634	89.4	36	78.3	0.02	595	89.9	75	80.7	<0.01
yes #	79	11.1	6	12.8		75	10.6	10	21.7		67	10.1	18	19.4	
Alcohol															
no #	707	98.9	45	95.7	0.12**	700	98.7	45	97.8	0.47**	654	98.8	91	97.9	0.35**
yes 8	8	1.1	2	4.3		9	1.3	1	2.2		8	1.2	2	2.2	
Probable Major Depression															
no #	619	86.8	42	89.4	0.62	618	87.4	37	80.4	0.17	581	88.0	75	81.5	0.08
yes #	94	13.2	5	10.6		89	12.6	9	19.6		79	12.0	17	18.5	
State Anxiety															
1st Q #	178	25.0	14	29.8	0.83	175	24.8	13	28.3	0.23	167	25.3	21	22.6	0.05
2nd Q #	189	26.5	10	21.3		185	26.2	13	28.3		171	26.0	27	29.0	
3rd Q #	179	25.1	12	25.5		185	26.2	6	13.0		176	26.7	15	16.1	
4th Q #	166	23.3	11	23.4		161	22.8	14	30.4		145	22.0	30	32.3	

*Chi-square test or Fisther's Exact Test for small cell counts.
**Fisher's Exact Test

Table 1.6 Odds ratios of preterm birth by level of perceived stress: Proyecto Buena Salud, 2006-2011

	Preterm Birth		Unadjusted		Adjusted Model 1		Adjusted Model 2		Adjusted Model 3		Adjusted Model 4[#]	
	n	%	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Early Pregnancy (n=858)*												
Stress - PSS continuous	85	9.9	1.00	0.97,1.03	1.01	0.97,1.04	1.01	0.97,1.04	1.04	0.99, 1.09	1.04	0.99, 1.09
Stress - PSS quartiles												
1st Quartile	31	11.6	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	20	10.5	0.90	0.50,1.63	0.92	0.49,1.73	0.92	0.49,1.73	0.91	0.47,1.76	0.91	0.47,1.76
3rd Quartile	16	7.7	0.64	0.34,1.21	0.69	0.35,1.33	0.69	0.35,1.33	0.74	0.35, 1.55	0.74	0.35, 1.55
4th Quartile	19	9.6	0.82	0.45,1.49	0.92	0.49,1.74	0.92	0.49,1.74	1.34	0.59, 3.06	1.34	0.59, 3.06
			P_{trend}=	0.31	P_{trend}=	0.56	P_{trend}=	0.56	P_{trend}=	0.86	P_{trend}=	0.86
Mid Pregnancy (n=792)												
Stress PSS score - continuous	72	9.1	1.02	0.99,1.06	1.03	0.99,1.07	1.03	0.99,1.06	1.06	1.01, 1.11	1.06	1.01, 1.11
Stress - PSS quartiles												
1st Quartile	14	6.5	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	17	8.7	1.36	0.65, 2.85	1.37	0.63, 2.97	1.57	0.70,3.54	1.79	0.78, 4.10	1.78	0.77, 4.12
3rd Quartile	22	11.3	1.82	0.90, 3.66	1.73	0.83, 3.61	1.80	0.82,3.94	2.54	1.10, 5.88	2.41	1.04, 5.60
4th Quartile	20	10.5	1.68	0.82, 3.43	1.95	0.93, 4.09	1.91	0.86, 4.24	3.87	1.53, 9.76	3.50	1.38, 8.87
			P_{trend}=	0.11	P_{trend}=	0.06	P_{trend}=	0.11	P_{trend}=	<0.01	P_{trend}=	<0.01

*Early Pregnancy
Model 1- maternal age, BMI, parity, history of PTB
Model 3- maternal age, BMI, parity, history of PTB, trait anxiety

**Mid Pregnancy
Model 1 - maternal age, BMI, parity, history of PTB
Model 2 - maternal age, BMI,parity, history of PTB, mid-pregnancy smoking
Model 3 - maternal age, BMI, parity, history of PTB, mid-pregnancy depression,mid-pregnancy state anxiety
Model 4 - maternal age, BMI, parity, history of PTB, mid-pregnancy smoking, mid-pregnancy state anxiety, mid-pregnancy depression

Table 1.7 Odds ratios of low birth weight by level of perceived stress: Proyecto Buena Salud, 2006-2011

PSS Score	Low Birth Weight		Unadjusted		Adjusted Model 1		Adjusted Model 2		Adjusted Model 3		Adjusted Model 4[#]	
	n	%	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Early Pregnancy*												
Stress - PSS continuous			1.00	0.96,1.03	1.01	0.98,1.05	1.01	0.98,1.05	1.07	1.01,1.12	1.07	1.01,1.12
Stress - PSS quartiles	63											
1st Quartile	20	7.5	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	18	9.7	1.33	0.68,2.58	1.66	0.82,3.36	1.66	0.82,3.36	1.93	0.91,4.08	1.93	0.91,4.08
3rd Quartile	13	6.3	0.83	0.40,1.72	1.08	0.50,2.33	1.08	0.50,2.33	1.49	0.57,3.28	1.49	0.57,3.28
4th Quartile	12	6.1	0.80	0.38,1.67	1.13	0.52,2.47	1.13	0.52,2.47	2.29	0.85,6.23	2.29	0.85,6.23
			P_{trend}=	0.39	P_{trend}=	0.95	P_{trend}=	0.95	P_{trend}=	0.16	P_{trend}=	0.16
Mid Pregnancy												
Stress - PSS continuous			1.04	1.00,1.08	1.04	1.00,1.08	1.04	1.00,1.08	1.04	1.00,1.08	1.04	1.00,1.08
Stress - PSS quartiles	57	7.2										
1st Quartile	10	4.7	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	11	5.8	1.24	0.52, 2.99	1.49	0.60,3.71	1.49	0.60,3.71	1.49	0.60,3.71	1.49	0.60,3.71
3rd Quartile	18	9.2	2.05	0.92,4.57	2.41	1.04,5.55	2.41	1.04,5.55	2.41	1.04,5.55	2.41	1.04,5.55
4th Quartile	18	9.5	2.11	0.95,4.70	2.53	1.10,5.82	2.53	1.10,5.82	2.53	1.10,5.82	2.53	1.10,5.82
			P_{trend}=	0.03	P_{trend}=	0.01	P_{trend}=	0.01	P_{trend}=	0.01	P_{trend}=	0.01
Late Pregnancy**												
Stress -PSS continuous			1.01	0.97,1.04	1.01	0.97,1.04	1.01	0.97,1.06	1.01	0.97,1.06	1.01	0.97,1.06
Stress - PSS quartiles	47	6.2										
1st Quartile	15	7.7	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	8	4.0	0.50	0.21,1.21	0.54	0.22,1.32	0.64	0.25,1.61	0.64	0.25,1.61	0.64	0.25,1.61
3rd Quartile	10	5.6	0.71	0.31,1.63	0.72	0.31,1.67	0.67	0.27,1.68	0.67	0.27,1.68	0.67	0.27,1.68
4th Quartile	14	7.4	0.96	0.45,2.04	0.95	0.44,2.06	1.11	0.50,2.49	1.11	0.50,2.49	1.11	0.50,2.49
			P_{trend}=	0.94	P_{trend}=	0.98	P_{trend}=	0.77	P_{trend}=	0.77	P_{trend}=	0.77

*Early Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity, acculturation
Model 2- same as model 1
Model 3- maternal age, pre-pregnancy BMI, parity, acculturation, trait anxiety
Model 4- same as model 3

**Mid Pregnancy
Model 1 - maternal age, pre-pregnancy BMI, parity
Model 2 -same as model 1
Model 3 - same as model 1
Model 4 -same as model 1

***Late Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity
Model 2 - maternal age, pre-pregnancy BMI, parity, pre-pregnancy alcohol
Model 3- same as model 2
Model 4- same as model 2

Table 1.8 Odds ratios of small for gestational age births by level of perceived stress: Proyecto Buena Salud, 2006-2011

PSS Score	Small for Gestational Age		Unadjusted		Adjusted Model 1		Adjusted Model 2		Adjusted Model 3		Adjusted Model 4[#]	
	n	%	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Early Pregnancy*												
Stress- PSS continuous			1.02	0.99,1.05	1.02	0.99,1.05	1.02	0.99,1.05	1.03	0.99,1.08	1.03	0.99,1.08
Stress - PSS quartiles	100	11.7										
1st Quartile	27	10.2	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	26	14.1	1.45	0.82,2.57	1.47	0.82, 2.65	1.47	0.82, 2.65	1.65	0.89, 3.07	1.65	0.89, 3.07
3rd Quartile	25	12.2	1.23	0.69,2.19	1.28	0.71, 2.32	1.28	0.71, 2.32	1.43	0.72, 2.83	1.43	0.72, 2.83
4th Quartile	22	11.2	1.11	0.61,2.02	1.16	0.63,2.13	1.16	0.63,2.13	1.14	0.51, 2.54	1.14	0.51, 2.54
			P_{trend}=	0.78	P_{trend}=	0.69	P_{trend}=	0.69	P_{trend}=	0.74	P_{trend}=	0.74
Mid Pregnancy**												
Stress - PSS continuous			1.00	0.97,1.03	1.00	0.97,1.04	1.00	0.97,1.04	0.98	0.95,1.02	0.98	0.95,1.02
Stress - PSS quartiles	94	11.9										
1st Quartile	27	12.7	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	20	10.5	0.81	0.44,1.49	0.93	0.48, 1.78	0.93	0.48, 1.78	0.89	0.46, 1.71	0.89	0.46, 1.71
3rd Quartile	25	12.8	1.01	0.56,1.80	1.18	0.64, 2.20	1.18	0.64, 2.20	1.03	0.54, 1.98	1.03	0.54, 1.98
4th Quartile	22	11.6	0.90	0.49,1.64	1.04	0.55, 1.97	1.04	0.55, 1.97	0.66	0.31, 1.42	0.66	0.31, 1.42
			P_{trend}=	0.89	P_{trend}=	0.73	P_{trend}=	0.73	P_{trend}=	0.42	P_{trend}=	0.42
Late Pregnancy**												
Stress - PSS continuous			1.01	0.98,1.04	1.01	0.98,1.04	1.01	0.98,1.04	1.01	0.98,1.04	1.01	0.98,1.04
Stress - PSS quartiles	94	12.4										
1st Quartile	27	13.9	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
2nd Quartile	19	9.6	0.66	0.35,1.23	0.70	0.37,1.32	0.70	0.37,1.32	0.70	0.37,1.32	0.70	0.37,1.32
3rd Quartile	16	9.0	0.61	0.32, 1.18	0.63	0.32, 1.23	0.63	0.32, 1.23	0.63	0.32, 1.23	0.63	0.32, 1.23
4th Quartile	32	16.9	1.26	0.72, 2.20	1.34	0.75, 2.38	1.34	0.75, 2.38	1.34	0.75, 2.38	1.34	0.75, 2.38
			P_{trend}=	0.43	P_{trend}=	0.35	P_{trend}=	0.35	P_{trend}=	0.35	P_{trend}=	0.35

*Early Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity
Model 2- maternal age, pre-pregnancy BMI, parity
Model 3- maternal age, pre-pregnancy BMI, parity, trait anxiety
Model 4- same as model 3

**Mid Pregnancy
Model 1 - maternal age, pre-pregnancy BMI, parity, generation in U.S.
Model 2- same as model 1
Model 3 - maternal age, pre-pregnancy BMI, parity, generation in U.S., mid-pregnancy depression
Model 4 - same as model 3

***Late Pregnancy
Model 1 - maternal age, pre-pregnancy BMI, parity
Model 2- same as model 1
Model 3 - same as model 1
Model 4 - same as model 1

Table 1.9 Odds ratios of PTB, LBW and SGA by perceived stress level among women not prescribed antidepressants during pregnancy: Proyecto Buena Salud, 2006-2011*

	Preterm Birth						Low Birth Weight						Small for Gestational Age					
			Unadjusted		Adjusted**				Unadjusted		Adjusted***				Unadjusted		Adjusted***	
	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Early Pregnancy Stress	845						836						836					
1st Quartile	28	10.7	1.00	ref	1.00	ref	19	7.3	1.00	ref	1.00	ref	25	9.7	1.00	ref	1.00	ref
2nd Quartile	20	10.6	0.99	0.54, 1.81	1.00	0.52, 1.89	18	9.8	1.37	0.70, 2.69	1.54	0.77, 3.09	26	14.1	1.54	0.86, 2.76	1.57	0.86, 2.85
3rd Quartile	16	7.9	0.71	0.37, 1.36	0.75	0.39, 1.47	13	6.5	0.87	0.42, 1.81	1.04	0.49, 2.22	25	12.4	1.33	0.74, 2.39	1.37	0.75, 2.50
4th Quartile	19	9.9	0.91	0.49, 1.69	1.02	0.53, 1.94	12	6.3	0.84	0.40, 1.78	1.02	0.47, 2.20	22	11.5	1.21	0.66, 2.22	1.26	0.68, 2.34
Mid Pregnancy Stress	772						764						765					
1st Quartile	13	6.1	1.00	ref	1.00	ref	9	4.3	1.00	ref	1.00	ref	27	12.8	1.00	ref	1.00	ref
2nd Quartile	16	8.3	1.40	0.65, 2.99	1.42	0.64, 3.16	11	5.9	1.40	0.57, 3.46	1.74	0.68, 4.49	20	10.7	0.82	0.44, 1.51	0.83	0.44, 1.57
3rd Quartile	20	10.6	1.82	0.88, 3.77	1.76	0.82, 3.79	17	9.0	2.22	0.96, 5.10	2.69	1.12, 6.47	25	13.2	1.04	0.58, 1.86	1.07	0.58, 1.95
4th Quartile	20	11.2	1.95	0.94, 4.04	2.34	1.09, 5.01	18	10.1	2.53	1.11, 5.77	3.14	1.31, 7.49	20	11.2	0.86	0.47, 1.60	0.92	0.49, 1.73
Late Pregnancy Stress							739						739					
1st Quartile	n/a	n/a	n/a	n/a	n/a	n/a	14	7.4	1.00	ref	1.00	ref	26	13.8	1.00	ref	1.00	ref
2nd Quartile	n/a	n/a	n/a	n/a	n/a	n/a	8	4.1	0.54	0.22, 1.31	0.58	0.24, 1.44	19	9.8	0.68	0.36, 1.28	0.72	0.38, 1.37
3rd Quartile	n/a	n/a	n/a	n/a	n/a	n/a	10	5.7	0.76	0.33, 1.75	0.77	0.33, 1.80	16	9.1	0.63	0.33, 1.22	0.65	0.33, 1.27
4th Quartile	n/a	n/a	n/a	n/a	n/a	n/a	14	7.7	1.05	0.49, 2.26	1.03	0.47, 2.25	32	17.7	1.35	0.77, 2.37	1.41	0.79, 2.52

*Note- only 31 participants were identified as either taking or prescribed antidepressants during pregnancy through EMR

**Adjusted for age, bmi, parity, history of preterm birth

***Adjusted for age, bmi, parity

Table 1.10 Odds ratios of PTB, LBW and SGA by stress stratified by depression and anxiety: Proyecto Buena Salud, 2006-2011*

	Preterm Birth					Low Birth Weight					Small for Gestational Age				
	n			Unadjusted		n			Unadjusted		n			Unadjusted	
PSS Score (continuous)	**Total**	**PTB**	**%**	**OR**	**95%CI**	**Total**	**LBW**	**%**	**OR**	**95%CI**	**Total**	**SGA**	**%**	**OR**	**95%CI**
Depression															
Early Pregnancy															
No Major Depression															
PSS	687	75.0	10.9	1.01	0.97, 1.05	680	53.0	7.8	1.01	0.97, 1.05	680	72	10.6	1.01	0.97, 1.05
Major Depression															
PSS	151	11.0	7.3	0.98	0.88, 1.09	149	9.0	6.0	1.01	0.90, 1.14	149	23	15.4	1.03	0.95, 1.11
Mid Pregnancy															
No Major Depression															
PSS	630	57	9.0	1.05	1.01, 1.10	624	43	6.9	1.05	1.00, 1.10	624	69	11.1	0.98	0.94, 1.02
Major Depression															
PSS	139	11	7.9	1.04	0.93, 1.18	138	12	8.7	1.03	0.92, 1.16	138	23	16.7	0.98	0.90, 1.07
Late Pregnancy															
No Major Depression															
PSS	n/a	n/a	n/a	n/a	n/a	655	37	5.6	0.98	0.93, 1.02	655	76	11.6	0.99	0.95, 1.02
Major Depression															
PSS	n/a	n/a	n/a	n/a	n/a	98	9	9.2	1.07	0.95, 1.21	98	16	16.3	1.05	0.95, 1.15
Anxiety															
Early Pregnancy															
Not High Anxiety															
PSS	635	73	11.5	1.02	0.98, 1.06	627	53	8.5	1.03	0.98, 1.08	627	70	11.2	1.03	0.99, 1.07
High Anxiety															
PSS	220	13	5.9	1.09	0.98, 1.20	219	9	4.1	1.08	0.96, 1.22	219	29	13.2	1.01	0.94, 1.08
Mid Pregnancy															
Not High Anxiety															
PSS	458	47	10.3	1.05	1.00, 1.10	452	30	6.6	1.05	0.99, 1.11	452	51	11.3	0.99	0.95, 1.04
High Anxiety															
PSS	146	14	9.6	1.03	0.93, 1.13	146	11	7.5	1.01	0.91, 1.13	146	17	11.6	0.95	0.87, 1.04
Late Pregnancy															
Not High Anxiety															
PSS	n/a	n/a	n/a	n/a	n/a	577	32	5.5	0.96	0.91, 1.01	577	63	10.9	0.98	0.94, 1.02
High Anxiety															
PSS	n/a	n/a	n/a	n/a	n/a	175	14	8.0	1.07	0.99, 1.16	175	30	17.1	1.01	0.95, 1.07

*Odds ratios are for a unit increase in PSS score

Table 1.11 Odds ratios of PTB, LBW, and SGA by composite variables of stress with depression and anxiety: Proyecto Buena Salud, 2006-2011

	Preterm Birth							Low Birth Weight							Small for Gestational Age						
	n			Unadjusted		Adjusted*		n			Unadjusted		Adjusted**		n			Unadjusted		Adjusted**	
	Total	PTB	%	OR	95%CI	OR	95%CI	Total	LBW	%	OR	95%CI	OR	95%CI	Total	SGA	%	OR	95%CI	OR	95%CI
Stress and Depression																					
Early Pregnancy																					
not high stress/no major depression	589	63	10.7	1.00	ref	1.00	ref	582	47	8.1	1.00	ref	1.00	ref	582	64	11.0	1.00	ref	1.00	ref
not high stress/major depression	58	4	6.9	0.62	0.22, 1.77	0.52	0.16, 1.77	56	3	5.4	0.64	0.19,2.14	0.73	0.22,2.48	56	10	17.9	1.76	0.85,3.66	1.94	0.92,4.11
high stress/no major depression	98	12	12.2	1.17	0.60, 2.25	1.22	0.61, 2.46	98	6	6.1	0.74	0.31,1.79	0.79	0.33,1.92	98	8	8.2	0.72	0.33,1.55	0.73	0.34,1.58
high stress/major depression	93	7	7.5	0.68	0.30, 1.53	0.83	0.36, 1.92	93	6	6.5	0.79	0.33,1.89	0.90	0.22,2.46	93	13	14.0	1.32	0.69,2.50	1.32	0.69,2.53
Mid Pregnancy																					
not high stress/no major depression	543	46	8.5	1.00	ref	1.00	ref	537	34	6.3	1.00	ref	1.00	ref	537	62	11.6	1.00	ref	1.00	ref
not high stress/major depression	45	3	6.7	0.77	0.46, 2.20	0.63	0.18, 2.21	44	3	6.8	1.08	0.32, 3.68	1.07	0.31, 3.66	44	9	20.5	1.97	0.90, 4.29	2.14	0.96, 4.74
high stress/ no major depression	87	11	12.6	1.56	0.78, 3.15	1.93	0.93, 4.00	87	9	10.3	1.71	0.79, 3.70	1.89	0.86, 4.15	87	7	8.1	0.67	0.30, 1.52	0.66	0.29, 1.51
high stress/major depression	94	8	8.5	1.01	0.46, 2.20	1.06	0.47, 2.36	94	9	9.6	1.57	0.73, 3.38	1.62	0.74, 3.54	94	14	14.9	1.34	0.72, 2.51	1.54	0.81, 2.92
Late Pregnancy																					
not high stress/no major depression	n/a	n/a	n/a	n/a	n/a	n/a	n/a	544	32	5.9	1.00	ref	1.00	ref	544	60	11.0	1.00	ref	1.00	ref
not high stress/major depression	n/a	n/a	n/a	n/a	n/a	n/a	n/a	22	1	4.6	0.76	0.10, 5.85	0.67	0.09, 5.18	22	2	9.1	0.81	0.18, 3.54	0.80	0.18, 3.59
high stress/no major depression	n/a	n/a	n/a	n/a	n/a	n/a	n/a	111	5	4.5	0.76	0.29, 1.98	0.75	0.28, 1.99	111	16	14.4	1.36	0.75, 2.46	1.44	0.78, 2.63
high stress/major depression	n/a	n/a	n/a	n/a	n/a	n/a	n/a	76	8	10.5	1.88	0.83, 5.85	1.75	0.76, 4.02	76	14	18.4	1.82	0.96, 3.45	1.85	0.95, 3.59
Stress and Anxiety																					
Early Pregnancy																					
not high stress/not high anxiety	575	65	11.3	1.00	ref	1.00	ref	567	48	8.5	1.00	ref	1.00	ref	567	65	11.5	1.00	ref	1.00	ref
not high stress/high anxiety	86	2	2.3	0.19	0.05,0.78	0.19	0.05,0.80	85	2	2.4	0.26	0.06,1.09	0.29	0.07, 1.21	85	12	14.1	1.27	0.65, 2.46	1.41	0.72, 2.78
high stress/not high anxiety	60	8	13.3	1.21	0.55,2.65	1.13	0.48, 2.66	60	5	8.3	0.98	0.38,2.57	1.02	0.38, 2.70	60	5	8.3	0.70	0.27, 1.82	0.63	0.24, 1.65
high stress/high anxiety	134	11	8.2	0.70	0.36,1.37	0.84	0.42, 1.67	134	7	5.2	0.60	0.26, 1.35	0.68	0.30, 1.55	134	17	12.7	1.12	0.63, 1.99	1.21	0.68, 2.17
Mid Pregnancy																					
not high stress/not high anxiety	401	39	9.7	1.00	ref	1.00	ref	395	24	6.1	1.00	ref	1.00	ref	395	46	11.7	1.00	ref	1.00	ref
not high stress/high anxiety	69	6	8.7	0.88	0.48, 2.40	0.76	0.30, 1.96	69	5	7.3	1.31	0.45, 3.28	1.26	0.46, 3.47	69	10	14.5	1.29	0.62, 2.69	1.35	0.64, 2.86
high stress/not high anxiety	57	8	14.0	1.52	0.67, 3.43	1.69	0.72, 3.95	57	6	10.5	1.82	0.71, 4.66	1.97	0.76, 5.16	57	5	8.8	0.73	0.28, 1.92	0.69	0.26, 1.83
high stress/high anxiety	77	8	10.4	1.08	0.36, 2.18	1.13	0.49, 2.61	77	6	7.8	1.21	0.52, 3.31	1.32	0.51, 3.40	77	7	9.1	0.76	0.33, 1.75	0.83	0.36, 1.95
Late Pregnancy																					
not high stress/not high anxiety	n/a	n/a	n/a	n/a	n/a	n/a	n/a	495	30	6.1	1.00	ref	1.00	ref	495	52	10.5	1.00	ref	1.00	ref
not high stress/high anxiety	n/a	n/a	n/a	n/a	n/a	n/a	n/a	69	3	4.4	0.71	0.21, 2.37	0.63	0.18, 2.13	69	10	14.5	1.44	0.70, 2.99	1.38	0.65, 2.89
high stress/not high anxiety	n/a	n/a	n/a	n/a	n/a	n/a	n/a	82	2	2.4	0.39	0.09, 1.65	0.37	0.09, 1.57	82	10	13.4	1.32	0.66, 2.65	1.32	0.65, 2.69
high stress/high anxiety	n/a	n/a	n/a	n/a	n/a	n/a	n/a	106	11	10.4	1.80	0.87, 3.71	1.73	0.83, 3.62	106	20	18.9	1.98	1.13, 3.49	2.08	1.16, 3.72

*adjusted for maternal age, pre-pregnancy BMI, parity, and history of preterm birth

**adjusted for maternal age, pre-pregnancy BMI, and parity

Table 1.12 Odds ratios of PTB, LBW and SGA by patterns of stress during pregnancy: Proyecto Buena Salud, 2006-2011

	Preterm Birth*								Low Birth Weight**								Small for Gestational Age**							
	PTB		Unadjusted		Adjusted		Adjusted 2***		LBW		Unadjusted		Adjusted		Adjusted 2***		SGA		Unadjusted		Adjusted		Adjusted 2***	
	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI
Change in PSS Score - Early to Mid Pregnancy																								
Change in PSS score - continuous	49	9.9	1.01	0.97,1.06	0.99	0.94,1.04	1.01	0.96, 1.06	32	6.5	1.05	0.99,1.11	1.05	0.99,1.11	1.01	0.95, 1.07	54	11.0	0.99	0.95, 1.03	0.99	0.95, 1.04	0.99	0.94,1.04
No Decrease in Stress																								
no	24	8.5	1.00	ref	1.00	ref	1.00	ref	13	4.7	1.00	ref	1.00	ref	1.00	ref	33	11.8	1.00	ref	1.00	ref	1.00	ref
yes	25	12	1.45	0.80, 2.61	1.22	0.65, 2.30	1.35	0.68, 2.67	19	9.1	2.04	0.98, 4.22	2.05	0.96, 4.38	2.14	0.94, 4.86	21	10.0	0.83	0.46, 1.48	0.86	0.47, 1.55	0.85	0.45, 1.61
Change in PSS Score - Mid to Late Pregnancy																								
Change in PSS score - continuous	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	21	5.4	1.02	0.95, 1.08	1.02	0.96, 1.08	1.04	0.98,1.12	45	11.5	1.01	0.97, 1.06	1.01	0.96, 1.06	1.02	0.97, 1.07
No Decrease in Stress																								
no	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	13	5.6	1.00	ref	1.00	ref	1.00	ref	26	11.3	1.00	ref	1.00	ref	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	8	5.0	0.88	0.36, 2.17	0.92	0.37, 2.32	1.24	0.46, 3.33	19	11.8	1.06	0.57, 1.98	1.08	0.57, 2.07	1.17	0.97, 1.06
Change in PSS Score - Early to Late Pregnancy																								
Change in PSS score - continuous	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	28	5.7	1.01	0.96, 1.07	1.01	0.95, 1.06	1.02	0.96, 1.08	55	11.2	1.02	0.98, 1.06	1.03	0.99, 1.07	1.05	1.00, 1.09
No Decrease in Stress																								
no	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	16	5.3	1.00	ref	1.00	ref	1.00	ref	30	9.9	1.00	ref	1.00	ref	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	12	6.3	1.21	0.56, 2.62	1.12	0.51, 2.45	1.24	0.55, 2.82	25	13.2	1.38	0.78, 2.43	1.41	0.80, 2.51	1.65	0.90, 3.01
Cumulative Stress Across Pregnancy																								
High Stress Across Early and Mid Periods																								
none	34	10.4	1.00	ref	1.00	ref	n/a	n/a	22	6.8	1.00	ref	1.00	ref	n/a	n/a	39	12.1	1.00	ref	1.00	ref	n/a	n/a
one pregnancy period	10	9.1	0.86	0.41, 1.81	1.00	0.46, 2.18	n/a	n/a	7	6.4	0.93	0.39, 2.24	0.96	0.39, 2.37	n/a	n/a	10	9.1	0.73	0.35, 1.51	0.68	0.32, 1.45	n/a	n/a
both pregnancy periods	5	8.9	0.85	0.32, 2.26	0.94	0.34, 2.64	n/a	n/a	3	5.4	0.78	0.22, 2.68	0.81	0.81, 2.86	n/a	n/a	5	8.9	0.71	0.27, 1.90	0.83	0.31, 2.23	n/a	n/a
High Stress Across Early and Late Periods																								
none	n/a		n/a	n/a	n/a	n/a	n/a	n/a	18	5.8	1.00	ref	1.00	ref	n/a	n/a	28	9.0	1.00	ref	1.00	ref	n/a	n/a
one pregnancy period	n/a		n/a	n/a	n/a	n/a	n/a	n/a	5	4.2	0.72	0.26, 1.99	0.80	0.28, 2.24	n/a	n/a	18	15.3	1.82	0.97, 3.43	1.99	1.03, 3.82	n/a	n/a
both pregnancy periods	n/a		n/a	n/a	n/a	n/a	n/a	n/a	5	7.8	1.38	0.49, 3.86	1.58	0.55, 4.55	n/a	n/a	9	14.1	1.65	0.74, 3.70	1.80	0.79, 4.12	n/a	n/a

*adjusted for maternal age, pre-pregnancy BMI, parity and history of preterm birth

**adjusted for maternal age, pre-pregnancy BMI, and parity

***Adjusted model additionally adjusted for PSS in earliest period included in change

Table 1.13 Odds ratios of subtypes of preterm birth by levels of perceived stress: Proyecto Buena Salud, 2006-2011

	Preterm Birth Type																Spontaneous							
	Spontaneous				Medically Indicated				Preterm Labor				PPROM				Preterm Birth Gestational Age							
			Unadjusted				Unadjusted				Unadjusted				Unadjusted		Early (<34 weeks)		Unadjusted		Late (34-36 weeks)		Unadjusted	
	n	%	OR	95%CI	n	%	OR	95%CI	n	%	OR	95%CI	n	%	OR	95%CI	n	%	OR	95% CI	n	%	OR	95%CI
Early Pregnancy																								
Stress - PSS quartiles																								
1st Quartile	21	8.1	1.00	ref	10	4.1	1.00	ref	13	5.2	1.00	ref	8	3.3	1.00	ref	8	3.3	1.00	ref	23	8.9	1.00	ref
2nd Quartile	15	8.1	1.00	0.50, 1.99	4	2.3	0.56	0.17, 1.81	10	5.6	1.07	0.46, 2.50	5	2.9	0.87	0.28, 2.71	8	4.5	1.39	0.51, 3.79	12	6.6	0.73	0.35, 1.50
3rd Quartile	12	5.9	0.71	0.34, 1.48	4	2.1	0.50	0.15, 1.61	8	4.0	0.76	0.31, 1.88	4	2.1	0.62	0.18, 2.09	4	2.1	0.62	0.18, 2.09	12	5.9	0.65	0.31, 1.34
4th Quartile	16	8.3	1.01	0.52, 2.00	3	1.7	0.40	0.11, 1.47	13	6.8	1.33	0.60, 2.94	3	1.7	0.50	0.13, 1.91	6	3.3	1.00	0.34, 2.93	13	6.8	0.75	0.37, 1.53
Mid Pregnancy																								
Stress - PSS quartiles																								
1st Quartile	12	5.7	1.00	ref	2	1.0	1.00	ref	6	2.9	1.00	ref	6	2.9	1.00	ref	2	1.0	1.00	ref	12	5.7	1.00	ref
2nd Quartile	13	6.8	1.22	0.54, 2.74	3	1.7	1.69	0.28, 10.20	9	4.8	1.69	0.59, 4.83	4	2.2	0.75	0.21, 2.70	4	2.2	2.25	0.41, 12.42	13	6.8	1.22	0.54, 2.74
3rd Quartile	15	8.0	1.45	0.66, 3.17	7	3.9	4.05	0.83, 19.73	11	6.0	2.12	0.77, 5.85	4	2.3	0.77	0.21, 2.78	8	4.4	4.62	0.97, 22.07	14	7.5	1.35	0.61, 2.99
4th Quartile	16	8.6	1.57	0.72, 3.41	4	2.3	2.35	0.43, 13.00	7	4.0	1.37	0.45, 4.16	9	5	1.77	0.62, 5.06	4	2.3	2.35	0.43, 13.01	16	8.6	1.57	0.72, 3.41

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CHAPTER 2

DEPRESSSION AND ADVERSE BIRTH OUTCOMES AMONG PREGNANT HISPANIC WOMEN

Introduction

Preterm birth (<37 weeks gestation) and low birth weight (<2500 grams) are among the leading causes of infant mortality and morbidity in the United States.[1, 2] Though rates of these adverse birth outcomes are generally lower among Hispanic women, they differ by Hispanic ethnic subgroup with Puerto Rican women experiencing disproportionately high rates of these adverse birth outcomes as compared to non-Hispanic Whites.[3, 4] In addition, as disorders associated with preterm birth and low birth weight are the leading cause of infant mortality among Puerto Rican women,[1] it is important to identify risk factors that can be addressed to prevent these adverse birth outcomes in this population.

Depression during pregnancy has been identified as a potential risk factor for preterm birth and growth restriction during pregnancy, which includes both low birth weight and small-for-gestational age (SGA). Depressive disorders are common during pregnancy, affecting up to 18% of women.[5] These rates are reflective of the high rates of depression experienced among women of childbearing age. Depression relapse rates are particularly high during pregnancy, at approximately 43%, likely due to multiple factors, including: stress associated with pregnancy, hormonal changes occurring during pregnancy, and the decision to discontinue antidepressant maintenance medications made by some women or their clinicians.[6, 7] Rates of depression during pregnancy vary by

race/ethnicity,[8] with some studies among Hispanic populations finding estimates of probable depression as high as 33%.[9] Puerto Rican women may be more susceptible to depression than other Hispanic subgroups, as studies in the general population disaggregating rates of depression by Hispanic ethnic subgroups have found differences with Puerto Ricans having the highest lifetime prevalence among Hispanics.[10]

Proposed mechanisms describing how depression could lead to preterm birth, low birth weight, and small-for-gestational age (SGA) consist of both neurobiological pathways through hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system hormones, and behavioral pathways. In the case of preterm birth, the primary mechanisms include elevated levels of corticotrophin releasing hormone (CRH) and cortisol in depressed pregnant women that either directly or indirectly trigger early parturition, and unhealthy/risky health behaviors that are risk factors for preterm birth. These behaviors may occur either as a result of depression (e.g. smoking, alcohol consumption) or as a symptom of depression (e.g. poor appetite leading to inadequate nutrition). Primary proposed mechanisms for low birth weight and SGA also include elevated cortisol and catecholamine levels as potential mechanisms of action. Potential behavioral pathways are similar to those for preterm birth. It is possible that the potential neurobiological pathways involving CRH and cortisol would vary by race/ethnicity as some studies have found racial/ethnic differences in 1) HPA axis regulation and hormone levels during pregnancy,[11, 12] and 2) the manifestation of depression and related physiologic measures.[13]

The studies examining the association between depression and these adverse birth outcomes have been conflicting. Variability in study design, including both the

assessment of depression (e.g. instruments used, method of categorization) and categorization of the adverse birth outcomes (preterm birth, low birth weight, SGA) make it difficult to compare findings between studies and likely contribute substantially to the conflicting findings. Many of the studies also have a number of limitations, including: 1) small study sizes, 2) retrospective or cross-sectional design, 3) lack of consideration of confounders, 4) assessment of depression at a single timepoint during pregnancy, 5) use of depression assessment instruments that were developed for use in the general population that are likely to lead to misclassification in pregnant women, and 6) lack of consideration of other psychosocial factors (e.g. stress and anxiety) that may confound or modify the relationship between depression and each of the adverse birth outcomes. Finally, previous studies took place primarily in non-Hispanic White or Black populations with none focusing on a Hispanic population.

Therefore, this study extends the prior literature by prospectively examining the association between depression and preterm birth, low birth weight, and SGA among pregnant, primarily Puerto Rican Hispanic women, taking into account a number of potential confounding factors (sociodemographic, behavioral, acculturation and health). To our knowledge, this was the first study to examine this association in a Puerto Rican population. In addition, the effect of depression at various timepoints during pregnancy was assessed, as well as, the effects of patterns of depression during pregnancy. Potential confounding or interactive effects of other commonly co-occurring psychological factors (stress, anxiety) were also assessed. Finally, we minimized misclassification of depression during pregnancy that likely occurs in studies that used depression assessment instruments created for the general public by using the Edinburgh Postnatal Depression

Scale, which accounts for the overlap in physical symptoms common to both pregnancy and depression.

Physiological Mechanisms

Neurobiological Mechanisms

As depression has been associated with HPA axis dysregulation, including elevated levels of cortisol and CRH,[14, 15] it has been suggested that depression may lead to preterm birth, low birth weight, and SGA through neurobiological mechanisms similar to those in Chapter 1 describing how elevated stress levels may increase risk for these adverse birth outcomes.[16] Because cortisol and CRH levels are elevated in some individuals with depression, it is believed that stress and depression are interrelated. Some have argued that stress may precipitate depression in predisposed individuals,[14, 15] while others suggest that it is unclear whether stress is an etiologic factor or occurs in response to depression.[17] It is likely that the relationship between stress and depression is complex and that they are likely interrelated in both these ways depending on the individual and type of depression. For example, studies suggest that first lifetime depressive episodes are more highly associated with stress than recurrences of depression.[18] It is also important to note that HPA axis dysregulation is only observed in a subset of individuals with depression,[17] and subsequently, the proposed mechanisms involving HPA axis hormones would only be applicable in those experiencing elevated levels of these hormones. In addition, findings from some studies have found that HPA axis regulation and hormone levels during pregnancy may vary by race/ethnicity, leading some to suggest that these differences may mediate the association between

depression/stress and adverse birth outcomes, and thus partially explain racial/ethnic disparities.[11, 12]

Preterm Birth

As depression has been associated with elevated levels of CRH,[14] one of the primary proposed mechanisms describing how depression may be a risk factor for preterm birth is through early initiation of parturition triggered by these increased levels.[16] As described in Chapter 1, levels of CRH rise over the course of pregnancy and are thought to play a role in the initiation of parturition. Subsequently, premature elevation of CRH levels due to depression could lead to early parturition. It has also been suggested that elevated cortisol levels commonly observed in depressed individuals[14] increases risk for infection and, subsequently, preterm birth, as inflammation is associated with parturition.[16] Increased inflammation due to elevated plasma levels of proinflammatory cytokines associated with depression has also been suggested as a mechanism to partially explain the association between depression and preterm birth.[19]

Low Birth Weight and Small-for-Gestational Age

As in the case for the theorized neurobiological mechanisms explaining how stress may lead to the adverse birth outcomes of interest, those explaining how depression may lead to low birth weight and SGA are less clearly defined than those for preterm birth. Prolonged elevated levels of cortisol and norepinephrine are thought to be the primary mediators of depression and growth restriction. As cortisol levels are elevated in some individuals with depression, it has been suggested that these increased cortisol

levels inhibit fetal growth similar to the pathway described for the relationship between stress and growth restriction in Chapter 1.[16] In addition, the increased risk for infection caused by elevated cortisol levels described above provide another potential pathway as infection has been identified as a risk factor for low birth weight and growth restriction.[20] Finally, as some studies have found elevated levels of norepinephrine in depressed women during pregnancy,[21] it has been suggested that these elevated levels lead to decreased uterine perfusion subsequently restricting growth.[22]

Racial and Ethnic Differences in HPA Axis Regulation

Among the few studies conducted examining HPA hormone levels during pregnancy by race/ethnicity, some have found that hormone levels (CRH, adrenocorticotropic hormone, cortisol) and patterns of release of these hormones vary by race/ethnicity. For example, some studies have found lower CRH levels among Hispanic[23] and Black women[11, 24, 25] at various times during pregnancy compared to non-Hispanic White women. Differences in the associations between hormone levels over the course of pregnancy have also been observed with higher levels of cortisol at 18-20 weeks predicting CRH levels at 30-32 weeks among African American and Hispanic women but not non-Hispanic White women.[11] Finally, differences in the cumulative effect of stress on hormone levels has been found to vary according to race/ethnicity, with one study finding an association observed between cumulative stress and decreased cortisol levels and daytime pattern of release among pregnant Black women, but not Hispanic women.[12] These studies suggest the possibility of differences in HPA axis hormone levels and function during pregnancy by race/ethnicity. In addition, in one of

the few studies conducted looking at racial differences in the effect of depression during pregnancy, Field et al. found that depressed pregnant Hispanic women had higher levels of norepinephrine than African-American women after adjusting for SES.[26]

Behavioral Mechanisms

In addition to these neurobiological mechanisms, several behavioral mechanisms have also been proposed to explain how depression may increase risk for preterm birth, low birth weight and SGA.[16] Depression during pregnancy is associated with an increase in unhealthy/risky health behaviors, such as smoking and alcohol consumption during pregnancy, both of which have been identified as risk factors for preterm birth and growth restriction.[19, 20] In addition, as loss of appetite is a symptom of depression in some individuals, inadequate nutrition may be a mediator of these relationships as it is also a risk factor for preterm birth and growth restriction. Differences in prevalence of risky health behaviors and the associations of some of these behaviors with adverse birth outcomes across racial/ethnic groups may help to explain disparities in these adverse birth outcomes observed among some racial/ethnic groups.[27] Some have questioned whether these risky health behaviors are etiologic factors or confounders as some studies adjusting for these factors have still found an association between depression and preterm birth.[19] It is likely that depression increases risk for these adverse birth outcomes through a combination of behavioral and neurobiological pathways.

Prior Epidemiological Research

Preterm Birth

A number of studies have examined the relationship between depression during pregnancy and preterm birth with conflicting results. Of the 34 English language studies conducted since 1996 that examined the relationship between depression during pregnancy and PTB, [28-61] fifteen found that depression increased risk of PTB (odds ratios range 1.3-4.9)[43, 45-53, 56, 57, 62] or decreased GA at birth [44, 54, 58] while the remainder found no effect. [28, 30-42, 59-61, 63] All but one [49] were prospective studies. Methodological differences and potential limitations, which are discussed in more detail below, likely contributed to the conflicting findings. Despite these conflicting findings, the studies suggest a positive association between depression, particularly in early- to mid pregnancy, and preterm birth as null studies not finding a statistically significant association had several limitations, including, small sample sizes, which would bias the findings of those studies towards the null.

In a recent large cohort study, Kramer et al. examined the association between depression and spontaneous preterm birth among 5,337 women recruited through four large maternity hospitals in Montreal.[40] Depressive symptoms were assessed between 24 and 26 weeks gestation using the Centers for Epidemiologic Studies-Depression Scale (CES-D), with scores equal to or greater than 16 indicating depression. Spontaneous preterm birth cases were identified by monitoring the delivery wards and were defined as women delivering before 37 weeks gestation following spontaneous labor. Women who were depressed had 40% increased odds of spontaneous preterm birth compared to nondepressed women after adjusting for potential sociodemographic confounders and

medical and obstetric risks (OR=1.4, 95% CI=1.01,2.1). When pregnancy-related anxiety and perception of high pregnancy risk were added to the model as potential confounders, the association no longer existed.

This study had several limitations. One important limitation was the use of the CES-D to assess depression. The CES-D was developed for use and validated in the general population and includes questions about somatic depressive symptoms that are also common symptoms of pregnancy (e.g. fatigue, loss of appetite). Thus, use of this instrument and the cut-points chosen based on validation studies in the general population are likely to lead to nondifferential misclassification of depression, which would attenuate results. In addition, depression was only measured during one timepoint during pregnancy (mid-pregnancy). This provides a limited assessment of the association between depression and preterm birth, as it is possible that conflicting results may be due to the time period of exposure to depression or the cumulative exposure to depression during pregnancy. Finally, as the authors did not collect information on the racial/ethnic background of participants, it was not included in adjusted analysis or assessed as an effect modifier of the relationship between depression and preterm birth.

In another recent cohort study, Li et al. prospectively examined the association between depressive symptoms in early pregnancy and the risk of preterm birth among 791 multiethnic women (40% White, 7% African American, 22% Hispanic, 31% Asian) that were part of Kaiser Permanente Medical Care Program, an integrated healthcare delivery system.[48] The CES-D was used to assess depressive symptoms at approximately 10 weeks gestation with 16 or greater indicating "significant depressive symptoms" and 22 or greater indicating "severe depressive symptoms." Preterm delivery was identified

as women delivering before 37 weeks gestation. Women with extreme prematurity (<33 weeks) were excluded because of the likelihood that this outcome was due to other medical causes. A dose response association was observed after adjusting for a variety of confounders with women scoring between 16 and 21 on the CES-D having 60% increased risk of preterm birth (HR=1.6, 95% CI=0.7,3.6) and women scoring greater than 22 having more than twice the risk of preterm birth (HR=2.2, 95% CI=1.1,4.7, p-trend<0.01). Removal of CES-D questions querying depressive symptoms that are also common to pregnancy (e.g. fatigue) did not alter the association.

Analysis of effect modification by stress and race/ethnicity using interaction terms in the regression model did not find a significant effect. However, stratified analysis suggested that stress might modify the association between depressive symptoms and preterm birth. Women experiencing high levels of stressful life events had twice the risk of preterm birth associated with CES-D scores of 16 or greater (HR=2.1, 95%CI=1.0-4.6) as compared to women with low levels of stressful life events experiencing 20% increased risk (HR=1.2, 95% CI=0.3-4.3). When stratifying by race/ethnicity, none of the effect estimates were statistically significant, though the hazard ratio was greater among White women (HR=2.7, 95% CI=0.9,7.9) compared to other racial/ethnic groups, with the greatest difference found when compared to African Americans (HR=1.2, 95% CI=0.3-5.2). Examination of hospital records found that only 1.5% of the study population was prescribed antidepressants during the study period, leading the authors to conclude that antidepressants did not confound the relationship between depressive symptoms and preterm birth. Limitations of this study include lack of consideration of confounding or effect modification by other measures of psychological distress/stress

(e.g. anxiety) and assessment of depressive symptoms at one timepoint in pregnancy only (early pregnancy).

The above studies illustrate some of the variability in study design among studies examining the association between depression and preterm birth, including timing of assessment of depression (early vs. mid pregnancy) and categorization of preterm birth (spontaneous preterm births vs. all preterm births > 32 weeks gestational age). The considerable variation in the assessment of depression and categorization of preterm birth between studies likely contributes to conflicting findings when examining this association. Differences in the methods used to assess depression include variability in the depression measure assessed (e.g. depressive symptoms, elevated depressive symptoms, depression), the instrument used to assess depression (e.g. EPDS, CES-D, clinical diagnosis), and the pregnancy timeframe during which depression is assessed (early, mid-, late pregnancy). While some of these differences may lead to inconsistent study results due to true differences in biologic mechanism, such as the depression measure assessed or timing of assessment, some may lead to bias, such as differences in the instrument used. The majority of studies used measures that were not designed for, or validated for use, among pregnant women (e.g. CES-D, BDI, GHQ).[30-33, 33, 34, 36-40, 47-52, 54, 64-66] As discussed above, because these measures include questions assessing somatic symptoms of depression that are also common symptoms of pregnancy (e.g. fatigue, loss of appetite), the potential for nondifferential misclassification is high in these studies. Though some of these studies tried to account for this misclassification by increasing the cut-point on their instrument or conducting sensitivity analyses,[30, 33, 38, 48, 51] the majority did not. Studies using diagnosis of clinical depression[29, 53, 67] as the exposure

measure avoid this potential source of bias, but are still likely subject to potential nondifferential misclassification as studies suggest that depression during pregnancy may be underdiagnosed and undertreated.[68] Only 5 studies used the Edinburgh Postnatal Depression Scale (EPDS), the only instrument used to assess the association between depression and preterm birth that was specifically designed to account for somatic depressive symptoms that are also common symptoms of pregnancy.[41, 43, 46, 55, 56]

There was also variability in the assessment of preterm birth, which likely contributed to conflicting findings. Some studies examined preterm birth overall, while others focused specifically on spontaneous preterm births,[30, 40, 43, 51] as it has been suggested that the mechanisms leading to spontaneous preterm birth are different than those leading to medically indicated preterm births.[69] Also, though most studies used the commonly defined cut-point of 37 full weeks gestation to define preterm birth, some studies used a continuous gestational age measure,[37, 38, 54] while others chose to use different gestational age ranges when assessing this association.[30, 34, 48, 67]

The studies examining this association were also subject to a number of limitations in addition to those described above, which include: (1) small sample size,[31, 47, 53] (2) retrospective or cross-sectional data collection,[49] and (3) lack of consideration of confounders.[31, 36, 41, 53, 64, 67] In addition, none of the studies examined depression over multiple timepoints during pregnancy. As discussed above, this is important because it is possible that the effect of depression may vary depending on the timing[70] or pattern of depression/depressive symptoms during pregnancy. Also, very few studies included possible co-morbid psychological factors such as stress and anxiety in their analysis as potential confounders or effect modifiers.[32, 38, 40, 43, 48, 57] Finally, the studies primarily

focused on non-Hispanic White or Black women with only one study focusing on a Hispanic population, which was predominantly Mexican.[60]

Low Birth weight (LBW)

Studies examining the association between depression during pregnancy and low birth weight have also been conflicting. Of the 25 studies examined, the majority did not find an association [28-31, 36, 37, 41, 52-54, 57, 59, 71-74] while 9 found that depression increased risk for LBW (Odds Ratio Range: 1.4-2.2), or, similarly, decreased BW.[35, 39, 44, 45, 50, 55, 56, 58, 75] All but two of the studies [72, 74] were prospective.

In one of the largest studies conducted assessing this relationship, Evans et al. examined the association between depression and low birth weight among 13,194 predominantly Caucasian women that took part in the Avon Longitudinal Study of Parents and Children (ALSPC).[73] Depression was assessed at 18 and 32 weeks gestation with the EPDS. Low birth weight infants were defined as those born less than 2500 grams. Only term infants born between 37 and 43 weeks gestation were included in the analysis. Women that scored 13 or greater on the EPDS at 18 weeks gestation gave birth to babies that weighed 33.8 grams less than women scoring less than 13 in unadjusted analysis (95% CI=8.0-59.7). This effect was attenuated after adjustment for a variety of confounders, including gestational age (*B*=-1.0, 95% CI=-24.9,22.9). When restricting the analysis to women with 16 or greater on the EPDS, the effect was attenuated and was not statistically significant when compared to women that scored less than 13 (*B*=-22.5, 95% CI=-12.5-57.4) in adjusted multivariable analysis. Scoring a 13 or above on the EPDS increased odds of low birth weight by 57% compared to those scoring less than 13

at 18 weeks gestation after adjusting for gender, gestation and maternal age (OR=1.57, 95% CI=1.08-2.29). This effect was attenuated after adjusting for smoking (OR=1.38, 95%CI=0.94,2.01). Exposure to depression throughout pregnancy was associated with lower birth weight in unadjusted analysis with women scoring greater than 12 on the EPDS at 18 and 32 weeks giving birth to babies 40.2 grams lighter (95% CI=3.8,76.6). This effect was attenuated upon adjustment and was no longer statistically significant. This study has several limitations, including the use of an EPDS cut-points for major depression that differed from the recommended validated cut-point (recommended=15 or greater). In addition, the authors did not examine other psychosocial factors, such as stress and anxiety, as potential confounders or effect modifiers.

In another large cohort study examining this association, Neggers et al. examined the association between depression and low birth weight among 3,149 predominantly African-American low-income women.[50] Women receiving prenatal care at the local county health department were recruited for participation. Depression was assessed at 22-23 weeks gestation using a modified version of the CES-D that was included as part of a psychosocial questionnaire administered to participants. Scores above the median were used to categorize people with negative affect/depression. Low birth weight was defined as infants born weighing less than 2500 grams. Participants with negative affect/depression had 40% increased odds of low birth weight compared to those that did not have elevated scores after adjusting for a variety of potential confounders (OR=1.4, 95% CI=1.1-1.7). When stratified by BMI, the effect was only observed among women with low BMI (OR=1.5, 95% CI=1.1-2.3). This study was limited by the use of a modified version of the CES-D, which as described above, includes questions that may

not be valid for assessing depression in a pregnant population. It also used a median cut-point to assess elevated depressive symptoms (negative affect), which is a lower threshold than is typically used and not necessarily indicative of depression.

As exemplified by these studies, variability in the assessment of depression also exists in studies assessing the effect of depression on low birth weight. The majority of studies also used either unvalidated measures or instruments designed to assess depression in the general population (e.g. CES-D, BDI). In addition, there was variability in the measure used to assess low birth weight, with a number of studies assessing birth weight as a continuous variable[37, 41, 45, 53, 54] and one study examining the association between depression and low birth weight among term infants only.[73] In addition, the study focusing on term infants also adjusted for gestational age, which was not included in the other studies examining low birth weight as an outcome, and is more similar to SGA as it takes into account gestational age at birth. Lastly, similar limitations to those discussed above for depression and preterm birth are also present in studies of depression and low birth weight. They include: (1) small sample sizes,[31, 53] (2)retrospective design,[72, 74] and (3) lack of consideration of confounders.[31, 36, 41, 53, 71, 76] In addition, very few studies assessed depression at multiple timepoints, examined the effect of pattern of depression or duration of depression over the course of pregnancy,[73] or included consideration of stress or anxiety in the analysis.[43, 57] Finally, the majority of studies focused on non-Hispanic White or Black populations with no studies focusing primarily on a Hispanic population.

In summary, findings for the impact of depression on LBW have been conflicting, however, they are suggestive of the possibility of an increased risk. Differences in study

findings may be due to the wide range of depression measures as well as varying time points of assessment.

Small-for-Gestational Age

Studies examining the association between depression and SGA have also been conflicting with eight finding a positive association (OR Range: 1.05 – 3.02) [34, 38, 45, 77-79] and eight finding no association. [30, 50, 52, 55-58, 80-82] All but one [77] were prospective studies.

In a large cohort study that assessed this association, Goedhart et al. examined the relationship between depressive symptoms and SGA among 8,050 predominantly Caucasian women as part of the Amsterdam Born Children and their Development Study.[34] Women in Amsterdam were recruited at their first prenatal visit at approximately twelve weeks gestation. Depressive symptoms were assessed using the CES-D through a questionnaire sent to participants two weeks after recruitment. The commonly used cut-point of a score of 16 or greater was used to identify women at high risk for clinical depression or possible clinical depression. SGA was defined as a birth weight below the 10th sex- and parity-specific percentile based on standards from the Dutch Perinatal Registration, which includes information from national obstetric and neonatal databases. Women with elevated levels of depressive symptoms had 25% greater odds of SGA after adjusting for a variety of confounders (OR=1.25, 95% CI=1.07,1.45). This effect was attenuated when maternal smoking during pregnancy was added to the model (OR=1.19, 95% CI=1.02,1.39). Mediation analysis suggested that smoking was a partial mediator of the association between elevated depressive symptoms and SGA.

In the only study examining the association between depression and SGA among a racially/ethnically diverse population that included Puerto Rican women (29% Puerto Rican, 62% Black, 10% Non-Hispanic White), Steer et al. assessed the relationship between depressive symptoms, probable depressive disorders (probable dysphoria, probable depression) and SGA among 712 women aged 12-29 years.[66] Women recruited through prenatal clinics were assessed for depressive symptoms at 28 weeks gestation using the Beck Depression Inventory. Scores from 16-20 were categorized as indicative of dysphoria, and those 21 or greater were categorized as presumptive clinical depression. SGA was defined as birth weight below the 10th percentile based on standards adjusted for gestational age, ethnicity, maternal parity, and fetal sex. Among adult women (n=389), an increase in depressive symptoms (continuous) was associated with increased odds of SGA after adjusting for a variety of confounders (OR=1.05, 95% CI=1.01,1.11). No effect was found between depressive symptoms and SGA among adolescent women (n=323) (OR=0.97, 95% CI=0.89,1.06). Additional analyses conducted among adults found that women with probable dysphoria had over two times the odds of an SGA infant compared to women that did not have dysphoria, in adjusted analysis (OR=2.32, 95%CI=2.21,2.43). The effect was even greater among women with elevated BDI scores indicative of probable clinical depression (OR=3.02, 95%CI=2.88,3.17).

As illustrated by the above studies, similar study design variability exists in those studies examining the relationship between depression and SGA as that seen in studies of the other adverse birth outcomes. When assessing depression, two studies used the Structured Clinical Interview for Depression to identify women with Major Depressive Disorder,[45, 77] while the remaining studies used measures designed to assess depression in

the general population (e.g. CES-D, BDI, Hopkins Symptom Checklist).[30, 34, 38, 50, 66, 78, 80, 81, 83] There was also variability in the categorization of SGA, or intrauterine growth restriction, with some studies identifying cases based on age-specific birth weight standards;[30, 81] others, such as the studies described above, taking into account additional factors such as ethnicity, parity and sex;[34, 66] and yet others using different measures that take into account gestational age and weight, such as growth rate.[38]

Though study findings have been conflicting, studies suggest that early to mid-pregnancy depression may increase risk for SGA. Studies finding a positive association tended to focus on early-to-mid pregnancy depression, [34, 45, 56, 78] whereas those finding a null association generally focused on mid-to-late pregnancy depression.[30, 50, 57, 58, 80] However, a number of the studies conducted had limitations similar to those described for studies of preterm birth and low birth weight, including: (1) small sample size,[77] (2) retrospective design,[77] and (3) lack of consideration of confounders.[80] In addition, only three studies took into account the possible effects of stress/anxiety[57, 78, 83] on the association between depression and SGA and only two studies assessed depression at more than one timepoint during pregnancy or duration of exposure to depression during pregnancy.[38, 78]

Summary

Preterm birth and low birth weight are among the leading causes of infant morbidity and mortality in the United States,[1] disproportionately impacting Puerto Rican women.[3, 4] Infant mortality rates among Puerto Rican women due to these adverse birth

outcomes are double that of non-Hispanic White women, and are the leading cause of infant mortality among this Hispanic ethnic subgroup.[1]

Depression during pregnancy is common and has been identified as a potential risk factor for preterm birth, low birth weight, and SGA. Neurobiological theories proposed to explain how depression leads to these adverse birth outcomes have focused on elevated levels of CRH, cortisol, and epinephrine. Behavioral theories suggest that depression leads to risky health behaviors (e.g. smoking, inadequate nutrition), which in turn, increase risk for these adverse birth outcomes. As some studies focusing on pregnant Hispanic populations have found high depression rates and studies suggest the possibility that HPA hormone function may vary during pregnancy by race/ethnicity, it is important to examine the association between depression and these adverse birth outcomes in this high-risk population.

Though studies examining the association between depression and preterm birth, low birth weight, and SGA suggest the possibility of increased risk due to depression, they have been conflicting, likely due to variability in methods used to assess and categorize depression and the adverse birth outcomes. Many of the studies have also been subject to a number of limitations and few have examined the effect of depression beyond a single timepoint of exposure during pregnancy. In addition, the studies have focused primarily on non-Hispanic White or Black women with few focusing on Hispanic women.

Our study examined the association between depression and preterm birth, low birth weight, and SGA in a population of Hispanic, predominantly Puerto Rican women. We minimized potential misclassification of depression by using a depression assessment

instrument that takes into account symptoms of pregnancy and has been validated among pregnant women, the Edinburgh Postnatal Depression Scale. We also assessed the effect of depression at various timepoints during pregnancy, pattern of depressive symptoms, and duration of exposure to depression. In addition, we took into account the potential confounding effect of anxiety and interactive effects of stress and anxiety as we assessed these associations.

Hypotheses and Specific Aims

Specific Aim: To examine the association between depression during pregnancy and adverse birth outcomes among Hispanic women

Hypothesis 1a: Depression during pregnancy is positively associated with preterm birth

Hypothesis 1b: Depression during pregnancy is positively associated with low birth weight

Hypothesis 1c: Depression during pregnancy is positively associated with small-for-gestational age

Methods

Study Design and Population

Our study examined the association between depression during pregnancy and adverse birth outcomes using data from Proyecto Buena Salud (PBS), a prospective cohort study conducted from 2006-2011. The study was based at Baystate Medical Center, a large tertiary care center in Western Massachusetts, which has approximately

4,500 deliveries per year and serves an ethnically, socioeconomically diverse population. Details about the study design have been published previously.[84] PBS was approved by the University of Massachusetts, Amherst and Baystate Medical Center Institutional Review Boards.

Briefly, women were recruited in early pregnancy at prenatal care visits (up to 20 weeks gestation). All participants read and signed a written informed consent approved by the Institutional Review Boards at the University of Massachusetts-Amherst and Baystate Medical Center. Interviews were conducted by trained, bilingual interviewers in English or Spanish depending on patient preference. Eligibility for PBS was restricted to women of Puerto Rican or Dominican Republic ancestry, specifically, women that were either: 1) born in Puerto Rico or the Dominican Republic themselves; or 2) had at least one parent or both grandparents born at either of these two locations. As PBS was initially conducted to assess the relationship between pregnancy factors and gestational diabetes, other exclusion criteria included: multiple gestation; history of diabetes, hypertension, heart disease or chronic renal disease; less than 16 or greater than 40 years of age; and current use of medications thought to adversely affect glucose tolerance. Additionally, participants with antepartum fetal deaths were excluded. Women were interviewed at three timepoints during pregnancy: (1) early pregnancy (≤18 weeks gestation), (2) mid-pregnancy (19-26 weeks gestation), and (3) late pregnancy (>26 weeks gestation). For some women, interviews were not able to be conducted for all of the pregnancy periods.

At initial interview, participants completed a depressive symptoms questionnaire and provided information on sociodemographic, acculturation, behavioral, and

psychosocial factors. Information was updated at the two subsequent interviews. Medical records were abstracted after delivery for information on medical history, clinical characteristics of the pregnancy, and birth outcomes. Among the PBS participants, 1,262 met the study inclusion criteria and had information on depressive symptoms and the adverse birth outcomes of interest. Women were included if they had information on depressive symptoms from at least one pregnancy period. Eight hundred and forty-five participants had information on depression in early pregnancy, 781 in mid-pregnancy, and 764 in late pregnancy.

Assessment of Depression

The Edinburgh Postnatal Depression Scale (EPDS)[85] was used to assess depressive symptoms at each interview. The questionnaire was administered in English or Spanish depending on participant preference. The EPDS consists of 10 items asking respondents to indicate how frequently they have felt various mood states during the past seven days. Examples of items on the EPDS include, "I have been so unhappy that I have been crying," and "Things have been getting on top of me." Responses are on a 4-point scale ranging from "no, never" to "yes, most of the time" with corresponding scores of 0 (never) to 3 (most of the time). Scores are summed with total scores ranging from 0-30. Scores of 13 or higher are indicative of likely depression (minor or major) and those 15 or higher indicate likely major depression.[86] For each pregnancy period (early, mid, late), women were categorized as to whether or not they had any likely depression (minor or major), as well as, likely major depression. Imputation was used for the EPDS and other psychological measures included in this study (stress, anxiety) if participants were

missing fewer than 10% of items on the given scale.[32] Imputation consisted of replacing the missing value(s) with the participant's average score of the nonmissing items for the given scale. For the EPDS, a score was imputed if the participant was missing the value for one item on the scale. Depression scores were analyzed categorically (any likely depression, likely major depression) and with depressive symptoms as a continuous variable.

In addition, composite variables were created between depression and stress (no major depression/not high stress, major depression/not high stress, no major depression/high stress, major depression/high stress) and depression and anxiety (no major depression/not high anxiety, major depression/not high anxiety, no major depression/high anxiety, major depression/high anxiety) for each pregnancy time point to examine how stress and anxiety may affect the associations between depression and the adverse birth outcomes. Stress and anxiety were assessed using the Perceived Stress Scale (PSS)[87] and the Spielberger State-Trait Anxiety Inventory (STAI),[88] respectively. The 14-item version of the PSS scale was used, with scores for each item ranging from 0-4 and greater scores indicative of higher levels of perceived stress. The STAI consists of a trait and state anxiety scale, each consisting of 20 items scored from 1-4, with higher scores indicating higher levels of anxiety. The STAI was used to assess trait anxiety in early pregnancy and state anxiety in mid- and late pregnancy. PSS and STAI scores were categorized into quartiles. Participants were categorized as having "high" levels of stress or anxiety if their score for the given scale was in the top quartile of participant scores for that time period. All other women were categorized as having "not high" levels of the given psychological measure. Trait anxiety was used to create the early pregnancy

depression composite variable and the state anxiety scores were used to create the composite variables for mid- and late pregnancy depression.

Finally, the effects of patterns of depression/depressive symptoms on adverse birth outcomes was assessed by examining change in EPDS scores during pregnancy and duration of exposure to likely major depression during pregnancy. Change in EPDS score was examined continuously as the difference between the later pregnancy period EPDS score and the early pregnancy score, as a well as dichotomously, comparing women with an increase in EPDS scores during the course of pregnancy to women that did not have an increase in score. Duration of exposure was examined by assessing the number of pregnancy periods that a participant was categorized as having likely major depression across two pregnancy periods (e.g. early to mid-pregnancy, mid-to-late pregnancy). Duration of exposure to probable major depression could not be assessed across all three pregnancy periods due to the limited number of participants with EPDS information for all three pregnancy periods.

The EPDS has been validated as a depression screening tool in English speaking pregnant women[89] and as a post-natal depression screening tool among European Spanish women.[90] Recommended cut-off scores vary for postnatal and antenatal depression. The recommended cut-off score for antenatal depression in English speaking populations has been identified as ≥15 for major depression (sensitivity=100%; specificity=96-99%) and ≥13 for any depression (minor or major) (sensitivity=57%; specificity=98%) using Research Diagnostic Criteria assessed through Goldberg's Standardized Psychiatric Interview as the gold standard.[86, 91-93] These cut-points were used for this study as the majority of study participants were English speaking and no studies identified to date

have validated cut-points for antenatal depression in a Spanish speaking population. In addition, studies validating the EPDS for post-natal depression in Spanish-speaking populations using the recommended cut-points for English-speaking populations have found reasonable sensitivity and specificity for any depression (minor or major) (sensitivity=79%; specificity=96%) and major depression (sensitivity=83%; specificity=97%) when compared to DSM-IV criteria assessed through the Structured Clinical Interview for Axis I DSM Disorders.[90]

Assessment of Adverse Birth Outcomes

Preterm birth is defined as a birth occurring prior to 37 full weeks of gestation.[94] Cases of preterm birth were identified through medical record abstraction by a trained medical record abstractor. These cases were diagnosed by the hospital obstetricians based on their best clinical estimate, which was typically determined by: (1) ultrasound if available, and (2) last menstrual period when ultrasound information was not available. Information on gestational age at delivery and type of preterm birth was also collected through medical record abstraction. Type of preterm birth consisted of medically indicated and spontaneous preterm births. Medically indicated births are those births in which the physician initiates the labor and delivery process, and spontaneous births are those in which labor occurs spontaneously and include preterm labor or preterm premature rupture of the membranes (PPROM). Based on gestational age at delivery, preterm births were categorized as early (<34 weeks) and late (34-36 weeks). The study obstetrician confirmed all cases of preterm birth and their associated gestational age and preterm birth type.

Low birth weight infants were those with a birth weight less than 2500 grams at birth. SGA was defined as a birth weight less than the 10th percentile for gestational age.[94] Information on birth weight was abstracted from the medical record and was used to identify low birth weight infants. This birth weight and gestational age information was used to identify SGA infants by comparing these values to gestational age-specific infant birth weight reference values from a population-based Hispanic.[95]

Confounders

A number of sociodemographic, acculturation, behavioral, and physical and psychological factors were assessed as covariates. Information on sociodemographic and acculturation covariates was primarily obtained at the initial pregnancy interview. Sociodemographic covariates included maternal age, education level, income and whether the study participant was living with a partner. Level of acculturation covariates included 1) birthplace of participant, parents, and grandparents, and 2) overall degree of acculturation, which was assessed via the Psychological Acculturation Scale (PAS).[96] The PAS is a 10-item scale with responses ranging from 1-5 with lower scores reflective of a Hispanic/Latina orientation and higher scores indicative of an Anglo-American orientation. Average scores less than 3 were categorized as "low acculturation" and those greater than 3 as "high acculturation." Behavioral factors assessed included smoking and alcohol consumption; pre-pregnancy data on these behavioral factors was collected in addition to pregnancy data at each interview.

Physical and health history factors were obtained by self-report during the initial interview and through medical record abstraction and included: pre-pregnancy weight,

height, history of preterm delivery, parity, and history of intrauterine growth restriction. BMI was calculated using reported height and weight. A variable indicating history of preterm delivery or intrauterine growth restriction was created for inclusion in the low birth weight and SGA analyses. In addition, information on antidepressant use during pregnancy was obtained. Women were identified as taking antidepressants if 1) the electronic medical record indicated that they had reported taking antidepressants during their prenatal visits, or 2) the patient prescription database indicated that they were prescribed antidepressants during pregnancy.

Anxiety was also included as a potential covariate and was evaluated at each interview with the Spielberger State-Trait Anxiety Inventory (STAI).[88] Trait anxiety was assessed in early pregnancy and state anxiety in mid- and late pregnancy.

Data Analysis

The distributions of the early, mid- and late pregnancy depression measures and each of the adverse birth outcomes (preterm birth, low birth weight and SGA) were assessed. Mean EPDS scores across pregnancy were determined by 1) calculating the mean of EPDS score for all participants, and 2) calculating the mean of the participant mean scores. The frequency distribution of preterm births was examined for all preterm births, in addition to the preterm birth subcategories of type (spontaneous vs. medically indicated) and gestational age (early, late).

Bivariate analyses were conducted to examine the associations between covariates and depression and between covariates and each of the adverse birth outcomes. When examining the association between depression and the time varying covariates assessed

throughout pregnancy, which included the behavioral factors (smoking, alcohol consumption) and the other psychological measures (anxiety, depression), the value of the time varying covariate from the same pregnancy period as the depression measure was used. Trait anxiety was examined when assessing associations with early pregnancy depression, as a measure of early pregnancy state anxiety was not available. Chi-square tests, t-tests, and ANOVA were used as appropriate to evaluate associations with depression and with adverse birth outcomes. When expected cell counts for categorical variables were less than five, Fisher's Exact Test were conducted.

Multivariable logistic regression was used to assess whether depression during pregnancy was associated with each of the adverse birth outcomes. Early, mid- and late pregnancy depression levels were examined when assessing the associations with low birth weight and SGA. Only early and mid-pregnancy depression levels were included in the preterm birth analysis as a number of preterm births occurred before the late pregnancy interviews could be conducted. Age, BMI and parity were included as *a priori* confounders in regression models as they are known risk factors for preterm birth, low birth weight, and SGA. In addition, history of preterm birth was also included as an *a priori* confounder in the preterm birth analysis. Other potential confounders were included in the final models if the odds ratio between depression and the given adverse birth outcome changed by more than 10% when the confounder was included in the model. As in bivariate analyses, only time varying covariates from the same pregnancy period as the depression measure were assessed as confounders. If more than 35 participants were missing values for a given confounder, a missing category was used for that confounder in analyses.

Collinearity between depression and the psychological measures was assessed to ensure that it was appropriate to include stress and anxiety in adjusted models as depression commonly occurs with stress and anxiety. Findings from crosstabulations between depression and these measures, beta standard errors, and variance inflation factor (VIF) values from regression models indicated that an important degree of collinearity did not occur.

As in the Chapter 1 analysis examining the association between stress and adverse birth outcomes, a series of adjusted models were examined when assessing the association between depression and each adverse birth outcome. Adjusted Model 1 included potential sociodemographic, physical, health and acculturation confounders. Adjusted Model 2 included factors in Model 1 in addition to identified behavioral factors. These factors were included in separate analyses because of the possibility that they could be in the causal pathway by either leading to depression or increased depressive symptoms or occurring as a result of depression. Model 3 includes Model 1 factors and additionally adjusts for other psychological measures identified as confounders. Psychological measures were added to the model separately because of the possibility that they also may be in the causal pathway. Model 4 includes all identified confounders. Unadjusted analyses were also conducted examining the effect of depression on subcategories of preterm births (spontaneous, medically indicated, early and late).

As some women with depression may be treated with antidepressants and antidepressants have been found to be associated with adverse birth outcomes in some studies,[97] a sensitivity analysis was conducted examining the effect of depression on each of the adverse birth outcomes in a subset of patients that 1) did not have documented self-

reported antidepressant use during pregnancy in the electronic medical record database, or 2) that were not found to have been prescribed antidepressants during pregnancy in the hospital's electronic prescription database.

To examine whether the association between depression and the adverse birth outcomes varied by level of stress or anxiety, interaction terms were included in the regression models. However, due to limited sample size, errors occurred when running the models and we were not able to assess interaction using this method. Therefore, stratified analyses were conducted to examine the association between depression and each of the adverse birth outcomes by level of stress (high stress, not high stress) and anxiety (high anxiety, not high anxiety). In addition, we examined composite variables of depression and stress (no major depression/not high stress, major depression/not high stress, no major depression/high stress, major depression/high stress) and depression and anxiety (no major depression/not high anxiety, major depression/not high anxiety, no major depression/high anxiety, major depression/high anxiety) in regression analyses.

We also examined whether patterns of depressive symptoms/depression during pregnancy affected risk for adverse birth outcomes. The effect of change in depressive symptoms over the course of pregnancy was assessed in addition to the effect of duration of exposure to likely major depression. Change in depressive symptom score was examined from early to mid-, mid- to late, and early to late pregnancy for low birth weight and SGA. Only early to mid-pregnancy changes in EPDS score were examined when assessing the association with preterm births. Duration of exposure to major depression was examined from early to mid-pregnancy for all three birth outcomes, and from early to late and mid- to late pregnancy for low birth weight and SGA. Duration of

exposure to depression was examined as both a categorical and continuous variable. All analyses were conducted using SAS version 9.2 (SAS Institute Inc, Carey, NC).

Results

Study Population Characteristics

The mean age of study participants was 22.8 years (SD=5.0) with 70% of participants under 25 years of age (2.1). Forty-seven percent of participants were born in Puerto Rico or the Dominican Republic and 79.2% of the study population was categorized as having low levels of acculturation. Women were generally of low socioeconomic status with 58% of those that reported income having an income of less than $15,000 per year, and almost 48.8% of women reporting that they did not receive a high school diploma or GED. Fifty-one percent of participants reported living with a partner or spouse and 41.7% were nulliparous. Almost half of participants had a pre-pregnancy BMI classified as overweight or obese. Approximately a third of women reported smoking and 40% drinking alcohol in the year prior to pregnancy, with far fewer reporting these risk behaviors in early pregnancy. Mean early pregnancy stress scores were 26.1 (SD=7.1) and mean trait anxiety scores were 39.7 (SD=10.4).

The overall mean EPDS score during pregnancy was 8.29 (SD= 5.5). Mean depressive symptom scores were highest in early pregnancy and decreased over the course of pregnancy (2.2). Similarly, the percent of women with any likely depression was highest in early pregnancy (27.9%) and decreased throughout pregnancy (late pregnancy – 19.5%). Approximately, 18% of women were categorized as having likely

major depression in early and mid-pregnancy, with the percentage of women likely experiencing this disorder dropping to 13.0% in late pregnancy.

Among study participants, 9.4% had a preterm birth (n=119), 8.1% had an infant that was born low birth weight (n=101), and 12.7% an infant that was SGA (n=158)(2.3). Of the births born preterm, 75% were spontaneous and 70% were born between 34 and 36 weeks gestation (late preterm).

Depression and Covariates

In bivariate analyses examining the associations between depression during pregnancy and the potential covariates, education and income were associated with major depression (Table 2.4). Women that had major depression were more likely to have earned less than $15,000 per year and to have had an education level of "less than high school." This association was significant ($p<0.05$) or borderline significant ($p=0.06$-0.08) for all three pregnancy periods. In addition, a larger proportion of women with major depression in early pregnancy were between the ages of 20-29 than women that did not have major depression; though the differences did not quite reach statistical significance ($p=0.06$), the mean early pregnancy depressive symptoms were significantly higher among this age group ($p<0.01$). Age was not associated with major depression at any other time period. Women with major depression in mid-pregnancy were also less likely to be living with a partner or spouse than women that did not have major depression. A similar trend was observed for early pregnancy major depression, though it was not statistically significant. When examining pregnancy history, women with major depression in late pregnancy were more likely to have had a history of preterm

birth and have had two or more live births than women that did not have late pregnancy major depression. None of the acculturation factors were associated with major depression.

Women with major depression at any timepoint in pregnancy were more likely to have smoked in pre-pregnancy and during the corresponding time period than women that did not have major depression. In addition, major depression in early and late pregnancy was positively associated with alcohol use during the corresponding time period. Major depression at all timepoints was highly positively associated with trait anxiety and with stress and state anxiety for the corresponding time periods.

Adverse Birth Outcomes and Covariates

In bivariate analyses, women that had preterm births or low birthweight infants were more likely to have had a history of preterm birth and have smoked in mid-pregnancy than women that had a term birth (Table 2.5). Women with low birth weight infants were also more likely to have smoked in late pregnancy. No other factors were associated with preterm birth or low birth weight.

SGA was also associated with smoking. Women that gave birth to an SGA infant were more likely to have smoked in pre-, early or late pregnancy compared to women that did not give birth to an SGA infant. SGA was also found to be associated with parity, pre-pregnancy BMI, and education. Among women that had SGA infants, a larger proportion were nulliparous and identified as having a pre-pregnancy BMI below (less than 18.5) or within the normal range (18.5 – 25.0) as compared to women that did not have infants born SGA. In regards to education, women that had SGA infants were less

likely to have completed high school or its equivalency. Finally, the only other covariate associated with SGA was late pregnancy state anxiety, with a larger proportion of women having SGA infants in the highest quartile of state anxiety when compared to women that did not have an SGA infant.

Depression and Adverse Birth Outcomes

None of the depression measures assessed (major depression, any depression, depressive symptoms) were associated with preterm birth (Table 2.6) or low birth weight (Table 2.7) in unadjusted or adjusted analyses.

Early pregnancy depressive symptoms were associated with SGA in adjusted analyses controlling for health/sociodemographic factors and other psychological measures with a unit increase in EPDS score increasing risk for SGA by 5% (OR=1.05, 95% CI=1.00, 1.11)(Table 2.8). This increased risk was not observed in unadjusted analyses or analyses only adjusting for other sociodemographic/health measures; no behavioral factors were found to be confounders. Though risk for SGA was elevated among women with any likely early pregnancy depression (OR=1.78, 95% CI=0.90, 3.52) and those with major depression (OR=1.71, 95% CI=0.85, 3.46), neither of these depression measures were found to statistically significantly increase risk.

Mid-pregnancy depression increased risk for SGA in all adjusted analyses. Women with likely major depression had the greatest risk with 1.72 times the odds of SGA compared to women that did not have likely major depression (OR=1.72, 95% CI=1.02, 2.90) in analyses adjusting for health/sociodemographic factors. This risk became more pronounced after adjusting for other psychological measures (OR=1.82, 95% CI=1.01, 3.25). Women experiencing any likely depression were also at increased

risk as compared to women not experiencing any likely depression in adjusted analyses, though to a slightly lesser degree than women experiencing likely major depression. Similarly, mid-pregnancy depressive symptoms were also associated with SGA in adjusted analyses with 3% increased risk for each unit increase in the EPDS after adjusting for sociodemographic/health factors (OR=1.03, 95% CI=1.00, 1.07) and a 4% increased risk after additionally adjusting for psychological measures (OR=1.04, 95% CI=1.00, 1.09). Depression in late pregnancy was not associated with SGA.

Findings from studies that some antidepressants may increase risk for adverse birth outcomes have led some to suggest that antidepressant use may confound the association between depression and adverse birth outcomes. As we were not able to obtain antidepressant use information on all participants, a sensitivity analysis was conducted excluding the 31 women (2.4% of participants) that were identified as having likely taken antidepressants based on information from the electronic medical record database or the prescription database (Table 2.9). Findings were generally unchanged, with all of the mid-pregnancy depression measures associated with SGA in adjusted analyses. However, estimates of effect became more pronounced and mid-pregnancy major depression was significantly positively associated with SGA in unadjusted analyses as well (OR=1.74, 95% CI=1.03, 2.94). In addition, early pregnancy major depression also became significantly associated with SGA in adjusted analyses after removing women that likely took antidepressants during pregnancy (OR=1.68, 95% CI=1.00, 2.83).

Depression, Stress, Anxiety and Adverse Birth Outcomes

Analyses were conducted to determine whether the association between depression and the adverse birth outcomes varied by stress and trait and state anxiety levels. No differences were observed when stratifying by high and low stress and anxiety levels at any timepoint during pregnancy in unadjusted analyses (Table 2.10). However, this analysis was limited by sample size and limited power.

Composite variables of depression and stress and depression and anxiety were examined in unadjusted and adjusted analyses to better understand potential interactive or synergistic effects between these psychological factors (Table 2.11). Women that had both high trait anxiety and major depression in early pregnancy were at decreased risk for preterm birth in unadjusted analyses (OR=0.41, 95% CI=0.17, 0.91) as compared to women that did not have major depression and did not have high trait anxiety. This association was attenuated and no longer significant after adjusting for sociodemographic/health risk factors for preterm birth. Women experiencing major depression and high state anxiety in late pregnancy were at double the risk of SGA in unadjusted (OR=2.02, 95% CI=1.08, 3.77) and adjusted analyses (OR=2.08, 95% CI=1.08, 3.98) when compared to women that were not categorized as having likely major depression or high state anxiety.

Patterns of Depressive Symptoms and Adverse Birth Outcomes

When examining the effects of patterns of depressive symptoms on preterm birth, low birth weight and SGA, change in depressive symptom scores over the course of pregnancy was not significantly associated with any of the adverse birth outcomes (Table

2.12). Similarly, the dichotomous variable "increase in depressive symptoms" during pregnancy was not significantly associated with the adverse birth outcomes for any time period examined. When examining the effects of duration of exposure to major depression during pregnancy, risk for SGA increased by 59% for each additional pregnancy period of exposure to major depression across early and late pregnancy (OR=1.59, 95% CI=1.04, 2.44) and mid- and late pregnancy in adjusted analyses (OR=1.66, 95% CI=1.00, 2.74). When examining duration of exposure to depression during both of these time periods as a categorical variable in adjusted analyses, the effect estimate was elevated among women with increasing exposure, but the findings did not reach statistical significance. Duration of exposure to depression was not associated with SGA across early and mid-pregnancy or preterm birth or low birth weight for any timeframes examined.

Depression and Type of Preterm Birth

In unadjusted analyses examining the associations between depression and types of preterm birth, no associations were observed with spontaneous, medically indicated, or type of spontaneous preterm births (Table 2.13). Similarly, depression was not associated with preterm births categorized by gestational age. Power was limited when examining these associations.

Discussion

We found that women that were depressed in mid-pregnancy were at increased risk of having an SGA infant in adjusted analyses compared to women that were not

depressed during this time period in a prospective cohort study of Hispanic, predominantly Puerto Rican women. This association was observed for depressive symptoms as a continuous measure, any likely depression, and likely major depression in analyses that adjusted for sociodemographic/health factors and those that additionally adjusted for psychological factors. We also observed an increased risk for SGA among women with increasing levels of early pregnancy depressive symptoms in analyses that included adjustment for other psychological factors. This increased risk was not observed for the categorical measures of early pregnancy depression (any likely depression, likely major depression). Late pregnancy depression was not independently associated with increased risk for SGA. Our finding that depression increases the risk for SGA has been observed in some,[34, 45, 55, 77-79] but not all studies[30, 50, 52, 57, 58, 80-82] examining this association. Studies that have found this increased risk have generally observed this effect for early and mid-pregnancy depression, which corresponds to our findings.

Depression during pregnancy was not associated with low birth weight, which is consistent with the majority of studies conducted that have assessed this relationship.[28, 29, 31, 36, 37, 41, 52, 54, 57, 61, 71-73] Though low birth weight is also a measure of growth restriction, some infants are born low birth weight because they are born at a younger gestational age, and not due to growth restriction. This likely at least partially explains the difference in findings between SGA and low birth weight. Similarly, we did not find an association between depression during pregnancy and preterm birth. Study findings have been more conflicting when examining this association.

Few studies have examined the effect of depression on adverse birth outcomes among Hispanic populations. In one of the only studies to specifically focus on a Hispanic population, Ruiz et. al did not find that depressive symptoms directly increased the risk for preterm birth, though in structural equation modeling, they found that the interaction between depressive symptoms and the estriol/progesterone ratio predicted risk for preterm birth.[60] No studies to our knowledge examined the association between depression and low birth weight or SGA in a Hispanic population, which is important given that studies suggest that some physiologic mechanisms proposed to explain how depression may lead to growth restriction (e.g. HPA axis hormones) may possibly vary by race/ethnicity.

Women in our study experienced high rates of depression with 27.9% of women experiencing any likely depression and 18% experiencing likely major depression in early pregnancy, as compared to depression prevalence rates of 7.4% in early pregnancy found in one meta-analysis.[98] Similar high rates have been found in some studies focusing on Hispanic pregnant women. Our study participants were predominantly of low socioeconomic status (SES), which has been associated with increased prevalence of depression.[99] Low SES individuals often experience numerous stressors and have fewer resources to deal with the stressors, as reflected in our population with high levels of perceived stress (mean early pregnancy PSS=26.1, SD=7.1) as compared to estimates from a population sample of women (mean=20.2) or Hispanics (mean=21.3).[100] Experiencing these high levels of stress places them at increased risk for a depressive episode as studies suggest that major stress is associated with the first depressive episode.[101] As a history of depression is a major risk factor for a subsequent depressive

episode, these women are at increased risk for a depressive episode during pregnancy, and the subsequent potential effects on fetal development, including growth restriction.

Depression, Anxiety and Stress

This study is one of few to take into account anxiety and stress when examining the association between depression and adverse birth outcomes. We found that women that experienced both major depression and high anxiety in late pregnancy were at increased risk for SGA. We were unable to assess effect modification using interaction terms due to limited sample size. Several studies that have examined effect modification using interaction terms have not found an association.[32, 43, 48] It is not clear if there was power to detect effects. In the only other study identified that used composite variables to examine the combined effects of depression and anxiety on adverse birth outcomes, Ibaniz et al. did not find that women with high anxiety and depression in mid-pregnancy were at increased risk for SGA though an increased risk for preterm birth was observed among these women.[57]

Few studies have examined how psychological factors work synergistically and independently to affect adverse birth outcomes. The majority of studies have considered depression and other psychological factors without accounting for other psychological factors such as anxiety and stress. These factors often co-occur, and thus it is not clear when positive associations are found whether the risk is due to depression or co-morbid psychological factors.[102] In our study, we found that early pregnancy depressive symptom score was only statistically significantly associated with SGA after including other psychological measures found to be confounders, which in this case was trait

anxiety, in the model. Others have also attempted to isolate the effects of depression by adjusting for stress and anxiety.[40, 47, 78, 103] However, it is not clear that adjustment for stress is appropriate as stress may be a precipitating factor in the onset of depression, particularly in the first episode of major depression, as discussed previously.[101] We chose not to adjust for stress in our analyses for this reason. In addition, as the constructs for depression, anxiety and stress overlap, adjustment for stress and anxiety may adjust for part of the effect of depression and thus only certain components of depression may be assessed in these adjusted analyses. Finally, the measures used to assess the constructs underlying these psychological factors often overlap, and in the case of anxiety and depression, may at times result in poor discrimination between measures with one study finding that the trait scale of the STAI was more a measure of depression than anxiety.[104]

Patterns of Exposure to Depression

Few studies have examined the association between exposure to depression over multiple timepoints during pregnancy and adverse birth outcomes. This is important as a hypothesized mechanism for growth restriction includes prolonged exposure to hormones associated with depression - cortisol and norepinephrine. Our study found that increasing duration of exposure to likely major depression across early and late pregnancy increased risk for SGA. Two other studies were identified that examined this effect, both of which focused on birth weight as the outcome, taking into account gestational age at birth in their analyses. Evans et al. found that women that scored greater than 12 on the EPDS at 18 and 26 weeks gestational age gave birth at term to lower birth weight babies than women that did not score greater than 12 at either timepoint.[73] The effect was attenuated

and no longer statistically significant after adjustment. The EPDS cut-point used by Evans et al. is the cut-point recommended to identify women that have any depression, either minor or major.[86] It is possible that the effect was not as pronounced due to the inclusion of women with likely minor depression. Hoffman et al. specifically focused on study participants that had low occupational status and found that women experiencing elevated depressive symptoms in the second and third trimesters were at increased risk of having a baby born with a lower gestational age adjusted birth weight, as compared to women that did not have elevated symptoms in either trimester.[38] This association remained after adjustment for smoking, demographic and obstetric factors, but was attenuated and no longer significant after additional adjustment for stressors and social support. As discussed above, stress may lead to the onset of depressive symptoms, thus, adjustment may have partially reduced the effect of depression.

We did not find an association between increased depressive symptoms over the course of pregnancy and risk for any of the adverse birth outcomes. However, our simple size and power was limited as fewer participants had data for multiple timepoints over pregnancy. Our study was the first study to our knowledge to examine whether an increase in depressive symptoms increased risk for preterm birth, low birth weight or SGA.

Physiologic Mechanism

Several mechanisms have been proposed to explain how depression during pregnancy may lead to fetal growth restriction, primarily focusing on neuroendocrine and behavioral mechanisms. Hypothesized neuroendocrinological mechanisms are similar to

those postulated for how stress may increase risk for growth restriction as some studies have found higher levels of cortisol and norepinephrine among depressed pregnant women.[21] Women with a prior history of depression may be at increased risk because they are at higher risk of a depressive episode during pregnancy and studies also suggest that some individuals previously experiencing depressive disorder continue to experience a dysregulation of the HPA axis despite the absence of depressive symptoms.[105] Behavioral mechanisms focus on several risk/unhealthy behaviors, including smoking, inadequate nutrition, lack of prenatal care and heavy alcohol consumption. We found that likely major depression in early and mid-pregnancy increased risk for SGA, after considering smoking and alcohol consumption from the corresponding pregnancy period as potential confounders. More research is needed to understand the physiologic mechanisms by which depression leads to growth restriction.

Strengths and Limitations

Our study is one of few studies to examine the association between depression and adverse birth outcomes in a Hispanic population; in addition, it is one of few studies to examine depression at multiple timepoints during pregnancy and the effect of patterns of exposure to depression during pregnancy on adverse birth outcomes. Our study included adjustment for a number of confounders, which is lacking in some studies. Also, we used a measure of depression that takes into account depression symptoms that are also common symptoms of pregnancy. We also explored how depression may act in synergy with stress and anxiety to increase risk for adverse birth outcomes, and the independent effect of depression when taking into account anxiety.

Our study has several potential limitations. It is possible that misclassification of depression occurred as the EPDS has not been validated in a Spanish speaking population in the U.S. for antepartum depression screening.[91] Though the EPDS has been validated for post-partum depression in a Spanish speaking population from Spain using the English speaking cut-offs and found good sensitivity and specificity (at least minor: sensitivity=83%, specificity=97%; major: sensitivity=79%; specificity=96%),[90] differences in accuracy by descent and country of residence may occur as a result of slight differences in language and/or interpretation of terms and also cultural differences in the manifestation of depression.[106, 107] However, it is unlikely that this misclassification occurred to a large degree as the sensitivity and specificity of the Spanish version of the EPDS using the validated English language cut-points were good when assessing post-partum depression (at least minor: sensitivity=83%, specificity=97%; major: sensitivity=79%; specificity=96%).[90] As the English version of the EPDS has been demonstrated to have good sensitivity and specificity for detecting antenatal major depression (sensitivity=100%; specificity=96%), and reasonable sensitivity and specificity for detecting any likely antenatal depression (sensitivity=57%; specificity=98%), we anticipate relatively comparable sensitivity and specificity for the Spanish speaking version in this pouplation.[92]

It is also possible that there was misclassification of the adverse birth outcomes. As discussed in Chapter 1, there are several possible sources of nondifferential misclassification of preterm birth, low birth weight, and SGA. Though preterm births were identified from medical record review and verified by the study obstetrician, it is possible that misclassification occurred as gestational age is determined through the "best

clinical estimate," which most frequently used ultrasound and LMP. Both of these measures are estimates of "true" gestational age and differences would lead to nondifferential misclassification of preterm births, though we do not expect large differences between the "true" and obstetrician identified gestational age. Similarly, misclassification of gestational age would also occur when identifying SGA infants, as case status is determined by gestational age information in addition to birth weight. SGA would be subject to an additional potential source of nondifferential misclassification as the weight for gestational age cut-points used to identify SGA infants are based on a Hispanic population of varying descent[95] and studies have found that average birth weights may vary among Hispanics based on country of descent.[3] Another possible source of misclassification for SGA is the potential variation in birth weight measurement as the scales used to measure newborns likely have some measurement variability, though we anticipate this to be minimal as they are regularly calibrated. This would also be a potential source of misclassification for low birth weight.

It is also possible that selection bias occurred due to incomplete depression data on participants over the course of pregnancy and the possibility that women that experienced depression were more likely to drop out during the course of the study or not complete all three interviews. As discussed in Chapter 1, women that did not have mid-pregnancy exposure data had higher levels of trait anxiety, and trait anxiety is positively associated with mid-pregnancy depression. In addition, the prevalence of likely major depression in early pregnancy was slightly higher among women missing mid-pregnancy depression data (18.6%) when comparing to women with mid-pregnancy data (17.5%). SGA rates were also higher among participants missing mid-pregnancy depression data

(13.6%) than participants with mid-pregnancy data (11.9%). Thus, it is possible that women that did not have mid-pregnancy depression data were more likely to have major depression and give birth to an SGA infant, which would have lead to an underestimate of the association observed between mid-pregnancy depression and SGA.

Information bias was unlikely to have occurred as information on adverse birth outcome status was obtained through medical record abstraction by an abstractor blinded to the depression status of the participant. In addition, the study obstetrician that verified cases of preterm birth was also blinded to depression status. As this is a prospective study, information bias would have occurred if adverse birth outcome status was ascertained differentially for depressed and nondepressed participants.

Though we adjusted for a number of potential confounders of the relationship between depression and preterm birth, low birth weight and SGA, one important confounder that we were not able to adjust for was antidepressant use during pregnancy. As discussed in Chapter 1, some studies have shown that the use of antidepressants during pregnancy may independently increase risk of preterm birth, low birth weight and SGA,[97] though studies have not consistently demonstrated this effect.[108] We were able to obtain information on antidepressant use during pregnancy for some women, though the information was likely not complete as it was obtained from self-report identified through the medical record and electronic prescription databases, which would only have information for those women that were prescribed antidepressants from a Baystate provider. Thus, we conducted a sensitivity analysis excluding those women that likely used antidepressants as identified through these two methods, to see if the association between depression and SGA persisted once these women were removed. We found that

the association between mid-pregnancy depression persisted when excluding these women, and actually became more pronounced.

Another set of potential confounders that we did not adjust for were maternal pregnancy complications, such as gestational diabetes mellitus (GDM), gestational hypertension and pre-eclampsia. Generally, these conditions may increase risk for adverse birth outcomes, though in the case of GDM, risk for growth restriction may decrease as GDM may lead to macrosomia. It is possible that discovery of these conditions may lead to maternal depression in mid- to late pregnancy as they are typically diagnosed or manifest during this timeframe, which would lead to positive confounding. Though data was available for these conditions, we were unable to adjust for them in multivariable logistic regression analysis due to the rarity of occurrence leading to few or no participants in some strata. Therefore, we conducted a sensitivity analysis excluding participants with GDM, gestational hypertension or pre-eclampsia. We found that that association between mid-pregnancy depression and SGA was slightly attenuated and no longer significant. Though the findings were no longer significant, the estimate of effect remained the same for the depressive symptom score continuous measure.

One additional limitation to be considered relates to temporality. Our findings suggest that mid-pregnancy depression is associated with increased risk for having an SGA infant. However, it is possible that women that gave birth to an SGA baby learned of the growth restriction of their fetus during the course of pregnancy, which subsequently lead to depression.

The results of these studies may be generalizable to pregnant Hispanic women. As the hypothesized neurobiological mechanisms explaining the relationship between

depression and the adverse birth outcomes of interest primarily involve CRH and cortisol, factors limiting generalizability beyond Hispanic women are similar to those described when assessing the effect of stress on these adverse birth outcomes. Studies finding racial/ethnic variation in CRH levels, pregnant depressed women's norepinephrine levels, and fetal/neonatal activity and physiological markers among pregnant depressed women [11, 26] suggest the possibility that the relationship between depression and preterm birth, low birth weight, and SGA could vary for women from other racial/ethnic backgrounds, which would limit generalizability to women of other racial/ethnic backgrounds.

Conclusion

Few studies have examined the association between preterm birth, low birth weight and SGA among pregnant Hispanic women and none have focused on Puerto Rican women. We found that early pregnancy increases in depressive symptoms and mid-pregnancy depression increased risk for SGA in a population of pregnant Hispanic, predominantly Puerto Rican, low SES women. It is important to examine this association in this population due to their high risk for both depression and adverse birth outcomes. We also found that risk for SGA associated with depression increased after adjusting for anxiety and that longer duration of major depression during pregnancy increased risk for SGA. Our findings suggest that the relationship between depression during pregnancy and risk for adverse birth outcomes is complex. Most studies examining this association have only assessed depression at one timepoint during pregnancy and have not taken into account other psychological measures and thus may not capture the nuances of the associations between depression and adverse birth outcomes. More research is needed

that takes into account these factors and others to elucidate these complex relationships. As studies suggest that there may be racial/ethnic differences in the physiological mechanisms by which depression may increase risk for these adverse birth outcomes, it is important to examine these associations in these high-risk groups that experience disproportionately high rates of preterm birth and low birth weight so that strategies can be identified to reduce risk in these populations.

Table 2.1 Participant characteristics: Proyecto Buena Salud, 2006-2011 (n=1262)

	n	%
Maternal Age		
16-19	396	31.4
20-24	495	39.2
25-29	223	17.7
≥30	148	11.7
missing	0	
Pre-Pregnancy BMI		
less than 18.5	79	6.3
18.5-<25.0	601	48.0
25.0-<30.0	291	23.3
30 or greater	280	22.4
missing	11	
Education		
Less than high school	583	48.8
High school graduate or GED	388	32.5
Post high school	224	18.7
missing	67	
Income		
less than $15,000	357	30.2
$15,000-$30,000	182	15.4
$30,000 or greater	75	6.3
Don't Know/Refused	570	48.1
missing	78	
Parity		
0 live births	525	41.7
1 live birth	382	30.3
2 or more live births	352	28.0
missing	3	
Acculturation		
Low	897	79.2
High	236	20.8
missing	129	
Generation in U.S.		
Born in PR/DR	573	46.9
Parent born in PR/DR	578	47.3
Grandparent born in PR/DR	70	5.7
missing	41	
Live with partner/spouse		
no	575	48.7
yes	606	51.3
missing	81	
Smoking (pre-pregnancy)		
no	804	67.2
yes	392	32.8
missing	66	
Alcohol (pre-pregnancy)		
no	720	60.2
yes	476	39.8
missing	66	
Smoking (early pregnancy)		
no	722	86.0
yes	118	14.1
missing	422	

Table 2.1 Participant characteristics: Proyecto Buena Salud, 2006-2011 (n=1262) (continued)

	n	%
Alcohol (early pregnancy)		
no	819	97.4
yes	22	2.6
missing	421	
High Stress (4th Quartile) (early pregnancy)		
no	693	82.0
yes	152	18.0
missing	417	
High Trait Anxiety (4th Quartile) (early pregnancy)		
no	885	76.0
yes	280	24.0
missing	417	
Continuous Measure	**Mean**	**SD**
Stress	26.1	7.1
Trait Anxiety	39.7	10.4

Table 2.2 Distribution of depression in the study population: Proyecto Buena Salud, 2006-2011

Depressive Symptoms- Continuous	Mean	SD
Overall Pregnancy (n=1262)	8.3	5.5
Early Pregnancy (n=845)	9.1	5.9
Mid-Pregnancy (n=781)	8.4	6.1
Late Pregnancy (n=764)	7.4	5.8

Depression	Any Probable Depression		Probable Major Depression	
	n	%	n	%
Early Pregnancy (n=845)				
no	609	72.1	693	82
yes	236	27.9	152	18.0
Mid-Pregnancy (n=781)				
no	587	75.2	636	81.4
yes	194	24.8	145	18.6
Late Pregnancy (n=764)				
no	615	80.5	665	87
yes	149	19.5	99	13.0

Table 2.3 Distribution of birth outcomes in the study population: Proyecto Buena Salud, 2006-2011

		n	%
Preterm Birth* (n=1262)			
	Yes	119	9.4
	No	1143	90.6
Low Birth Weight (n=1248)**			
	Yes	101	8.1
	No	1147	91.9
Small for Gestational Age* (n=1248)**			
	Yes	158	12.7
	No	1090	87.3
Type of Preterm Birth			
Medically Indicated			
	Yes	29	2.5
	No	1143	97.5
Spontaneous			
	Yes	89	7.2
	No	1143	92.8
PPROM			
	Yes	34	2.9
	No	1143	97.1
Pre-term labor			
	Yes	55	4.6
	No	1143	95.4
Preterm Birth by Gestational Age			
Early preterm (<34 weeks)			
	Yes	36	3.1
	No	1143	97.0
Late preterm (34-36 weeks)			
	Yes	83	6.8
	No	1143	93.2

*gestational age <37 weeks
**less than 2,500 grams
***less than 10th sex-specific percentile of weight for gestational age

Table 2.4 Distribution of covariates by depression in the study population: Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (EPDS score- continuous)									Probable Major Depression														
	Early Pregnancy			Mid- Pregnancy			Late Pregnancy			Early Pregnancy					Mid-Pregnancy					Late Pregnancy				
										No		Yes		p-	No		Yes			No		Yes		p-
	mean	SD	p-value	mean	SD	p-value	mean	SD	p-value	n	%	n	%	value	n	%	n	%	p-value	n	%	n	%	value
Maternal Age																								
16-19	8.4	5.4	<0.01	8.5	5.9	0.81	7.1	5.1	0.83	244	35.2	38	25.0	0.06	197	31.0	42	29.0	0.45	211	31.7	22	22.2	0.26
20-24	9.8	6.0		8.2	6.0		7.5	6.0		246	35.5	66	43.4		258	40.6	52	35.9		271	40.8	44	44.4	
25-29	9.9	5.9		8.7	6.5		7.6	6.1		118	17.0	32	21.1		107	16.8	31	21.4		116	17.4	20	20.2	
>=30	7.8	6.6		8.2	6.2		7.2	6.4		85	12.3	16	10.5		74	11.6	20	13.8		67	10.1	13	13.1	
Pre-Pregnancy BMI																								
less than 18.5	9.0	5.6	0.25	8.2	6.0	0.37	8.1	6.4	0.24	36	5.2	9	6.0	0.15	45	7.2	9	6.3	0.56	40	6.1	9	9.1	0.28
18.5-<25.0	9.4	5.8		8.6	6.2		7.6	5.8		323	46.7	82	54.7		288	45.8	73	51.1		327	49.5	52	52.5	
25.0-<30.0	8.4	6.1		7.7	5.6		6.6	5.7		172	24.9	25	16.7		150	23.9	27	18.9		143	21.6	14	14.1	
30 or greater	9.1	6.0		8.6	6.4		7.5	5.8		160	23.2	34	22.7		146	23.2	34	23.8		151	22.8	24	14.2	
Education																								
Less than high school	9.8	6.4	<0.01	8.7	6.3	0.19	7.9	6.2	0.06	314	45.4	95	62.5	<0.01	285	47.2	76	56.7	0.08	189	45.4	57	60.0	0.03
High school graduate or GED	9.0	5.3		8.1	5.7		7.4	5.4		236	34.2	41	27.0		207	34.3	42	31.3		221	34.7	24	25.3	
Post high school	7.4	5.1		7.7	5.6		6.5	5.2		141	20.4	16	10.5		112	18.5	16	11.9		127	19.9	14	14.7	
Income																								
less than $15,000	10.1	6.2	<0.01	9.3	6.4	<0.01	8.4	6.4	<0.01	194	28.2	59	39.3	0.05	178	29.7	56	41.8	0.01	190	30.2	40	42.6	0.06
$15,000-$30,000	8.8	5.8		7.3	5.4		6.7	5.1		106	15.4	22	14.7		94	15.7	13	9.7		105	16.7	9	9.6	
$30,000 or greater	7.3	5.8		6.9	5.4		5.4	5.4		50	7.3	7	4.7		36	6.0	3	2.2		41	6.5	4	4.3	
Don't Know/Refused	8.8	5.7		8.1	5.9		7.3	5.6		338	49.1	62	41.3		291	48.6	62	46.3		293	46.6	41	43.6	
Parity																								
0 live births	8.5	5.7	0.03	8.0	5.8	0.43	6.8	5.3	0.08	298	43.1	57	38.0	0.44	271	42.7	51	35.2	0.25	278	41.9	29	29.6	<0.01
1 live birth	9.5	5.6		8.6	6.3		7.6	5.5		212	30.6	47	31.3		180	28.4	47	32.4		215	32.4	30	30.6	
2 or more live births	9.6	6.5		8.6	6.4		7.9	6.7		182	26.3	46	30.7		183	28.9	47	32.4		171	25.8	39	39.8	
History of Preterm Delivery																								
no	9.1	5.9	0.69	8.3	6.1	0.15	7.2	5.8	0.08	614	90.6	133	90.5	0.97	558	89.1	125	87.4	0.55	608	93.1	84	86.6	0.03
yes	9.4	5.8		9.3	6.0		8.6	6.2		64	9.4	14	9.5		68	10.9	18	12.6		45	6.9	13	13.4	
History of IUGR																								
no	9.1	5.9	0.71	8.3	6.1	0.11	7.4	5.8	0.65	653	99.4	140	100.0	1.00*	605	100.0	138	99.3	0.18*	632	99.7	94	100.0	1.00*
yes	8.0	6.1		18.0	n/a		5.5	3.5		4	0.6	0	0.0		0	0.0	1	0.7		2	0.3	0	0.0	
Uterine Infection during Pregnancy																								
no	9.1	5.9	0.27	8.3	6.1	0.004	7.3	5.8	0.261	678	99.3	145	98.6	0.360*	622	99.4	141	97.2	0.045*	657	99.4	95	99.0	0.493*
yes	11.6	7.4		14.6	4.9		10.2	6.3		5	0.7	2	1.4		4	0.6	4	2.8		4	0.6	1	1.0	
Placenta Previa during Pregnancy																								
no	9.1	5.9	0.47	8.4	6.1	0.692	7.4	5.8	0.673	680	99.1	146	99.3	1.000*	622	99.0	143	98.6	0.649*	657	99.1	96	100.0	1.000*
yes	8.1	7.1		7.5	6.0		5.7	2.8		6	0.9	1	0.7		6	1.0	2	1.4		6	0.9	0	0.0	
Acculturation																								
Low	9.1	5.9	0.75	8.4	6.0	0.28	7.5	5.8	0.81	533	79.6	113	78.5	0.77	464	80.0	109	83.9	0.32	474	78.6	70	76.9	0.72
High	8.9	6.0		7.8	5.9		7.4	6.0		137	20.5	31	21.5		116	20.0	21	16.2		129	21.4	21	23.1	

Table 2.4 Distribution of covariates by depression in the study population: Proyecto Buena Salud, 2006-2011 (continued)

	Depressive Symptoms (EPDS score- continuous)									Probable Major Depression													
	Early Pregnancy			Mid- Pregnancy			Late Pregnancy			Early Pregnancy					Mid-Pregnancy					Late Pregnancy				
										No		Yes		p-	No		Yes			No		Yes		p-
	mean	SD	p-value	mean	SD	p-value	mean	SD	p-value	n	%	n	%	value	n	%	n	%	p-value	n	%	n	%	value
Generation in U.S.																								
Born in PR/DR	8.8	5.8	0.08	8.1	6.2	0.19	7.3	5.9	0.42	323	48.7	61	40.9	0.07	294	47.7	63	46.0	0.12	298	46.4	43	43.9	0.45
Parent born in PR/DR	9.6	6.1		8.7	6.0		7.5	5.8		303	45.7	83	55.7		278	45.1	70	51.1		309	48.1	52	53.1	
Grandparent born in PR/DR	8.0	4.7		7.1	5.3		6.2	5.3		37	5.6	5	3.4		45	7.3	4	2.9		36	5.6	3	3.1	
Live with partner/spouse																								
no	9.6	6.0	0.03	8.8	6.3	0.04	7.6	6.0	0.48	328	47.7	83	55.0	0.11	277	46.3	77	57.9	0.02	306	48.8	50	52.6	0.49
yes	8.7	5.8		7.9	5.7		7.3	5.6		359	52.3	68	45.0		321	53.7	56	42.1		321	51.2	45	47.4	
Trait Anxiety																								
1st quartile	3.9	3.4	<0.01	3.6	3.6	<0.01	4.2	4.1	<0.01	210	30.4	2	1.3	<0.01	184	31.0	3	2.3	<0.01	204	33.3	5	5.3	<0.01
2nd quartile	6.5	3.5		6.5	4.4		6.1	4.4		207	30.0	3	2.0		162	27.3	9	6.8		165	26.9	7	7.5	
3rd quartile	10.3	3.8		9.3	4.9		8.7	5.5		176	25.5	28	18.7		149	25.2	30	22.7		137	22.4	26	27.7	
4th quartile	15.7	4.7		13.6	5.6		11.9	6.3		97	14.1	117	78.0		98	16.5	90	68.2		107	17.5	56	59.6	
Pre-Pregnancy																								
Smoking																								
no	8.5	5.7	<0.01	7.7	5.8	<0.01	6.7	5.3	<0.01	479	69.4	82	54.0	<0.01	428	70.6	73	53.7	<0.01	447	70.5	49	52.1	<0.01
yes	10.4	6.1		9.6	6.2		8.7	6.5		211	30.6	70	46.1		178	29.4	63	46.3		187	29.5	45	47.9	
Alcohol																								
no	8.6	5.9	<0.01	8.0	6.1	0.06	7.2	5.8	0.29	409	59.4	83	54.6	0.28	365	60.1	77	56.6	0.45	378	59.6	56	59.6	0.99
yes	9.8	5.8		8.8	5.9		7.7	5.9		280	40.6	69	45.4		242	39.9	59	43.4		256	40.4	38	40.4	
Early Pregnancy																								
Smoking																								
no	8.7	5.8	<0.01	n/a			n/a			605	87.9	117	77.0	<0.01	n/a					n/a				
yes	11.5	6.0		n/a			n/a			83	12.1	35	23.0		n/a					n/a				
Alcohol																								
no	9.0	5.9	0.01	n/a			n/a			675	98.0	144	94.7	0.04*	n/a					n/a				
yes	12.2	7.2		n/a			n/a			14	2.0	8	5.3		n/a					n/a				
Stress																								
1st quartile	4.8	3.8	<0.01	n/a			n/a			257	37.4	4	2.7	<0.01	n/a					n/a				
2nd quartile	7.6	4.5		n/a			n/a			171	24.9	15	9.9		n/a					n/a				
3rd quartile	10.8	4.9		n/a			n/a			161	23.4	39	25.8		n/a					n/a				
4th quartile	14.8	5.2		n/a			n/a			98	14.3	93	61.6		n/a					n/a				
Mid-Pregnancy																								
Smoking																								
no	n/a			8.0	5.9	<0.01	n/a			n/a					571	90.2	109	75.7	<0.01	n/a				
yes	n/a			10.9	6.9		n/a			n/a					62	9.8	35	24.3		n/a				
Alcohol																								
no	n/a			8.3	6.1	0.14	n/a			n/a					625	99.1	142	98.6	0.65*	n/a				
yes	n/a			11.5	5.6		n/a			n/a					6	1.0	2	1.4		n/a				

Table 2.4 Distribution of covariates by depression in the study population: Proyecto Buena Salud, 2006-2011 (continued)

		Depressive Symptoms (EPDS score- continuous)									Probable Major Depression													
		Early Pregnancy			Mid- Pregnancy			Late Pregnancy			Early Pregnancy					Mid-Pregnancy					Late Pregnancy				
											No		Yes			No		Yes			No		Yes		
		mean	SD	p-value	mean	SD	p-value	mean	SD	p-value	n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
Stress																									
	1st quartile	n/a			3.2	3.0	<0.01	n/a			n/a					208	32.9	1	0.7	<0.01	n/a				
	2nd quartile	n/a			6.6	4.1		n/a			n/a					187	29.5	7	4.9		n/a				
	3rd quartile	n/a			9.8	5.0		n/a			n/a					151	23.9	37	25.9		n/a				
	4th quartile	n/a			14.5	5.5		n/a			n/a					87	13.7	98	68.5		n/a				
State Anxiety																									
	1st quartile	n/a			3.6	3.5	<0.01	n/a			n/a					174	34.8	3	2.8	<0.01	n/a				
	2nd quartile	n/a			5.9	4.1		n/a			n/a					121	24.2	5	4.6		n/a				
	3rd quartile	n/a			9.1	5.2		n/a			n/a					130	26.0	28	25.9		n/a				
	4th quartile	n/a			14.3	5.1		n/a			n/a					75	15.0	72	66.7		n/a				
Late Pregnancy																									
Smoking																									
	no	n/a			n/a			7.0	5.5	<0.01	n/a					n/a					604	91.0	74	74.8	<0.01
	yes	n/a			n/a			10.4	7.2		n/a					n/a					60	9.0	25	25.3	
Alcohol																									
	no	n/a			n/a			7.3	5.7	<0.01	n/a					n/a					659	99.3	94	95.0	<0.01*
	yes	n/a			n/a			13.4	8.8		n/a					n/a					5	0.8	5	5.1	
Stress																									
	1st quartile	n/a			n/a			2.7	2.7	<0.01	n/a					n/a					194	29.3	1	1.0	<0.01
	2nd quartile	n/a			n/a			5.7	3.8		n/a					n/a					197	29.7	3	3.0	
	3rd quartile	n/a			n/a			8.1	4.7		n/a					n/a					161	24.3	19	19.2	
	4th quartile	n/a			n/a			13.4	5.5		n/a					n/a					111	16.7	76	76.8	
State Anxiety																									
	1st quartile	n/a			n/a			3.3	3.2	<0.01	n/a					n/a					194	29.4	1	1.0	<0.01
	2nd quartile	n/a			n/a			5.2	4.0		n/a					n/a					193	29.2	5	5.1	
	3rd quartile	n/a			n/a			8.0	4.6		n/a					n/a					172	26.0	18	18.2	
	4th quartile	n/a			n/a			13.7	5.5		n/a					n/a					102	15.4	75	75.8	

* Fisher's Exact Test

Table 2.5 Distribution of covariates by birth outcomes in the study population: Proyecto Buena Salud, 2006-2011

	Preterm Birth (n=1262)					Low Birth Weight (n=1248)					Small for Gestational Age (n=1248)				
	No		Yes			No		Yes			No		Yes		
	n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
Maternal Age															
16-19	354	31.0	42	35.3	0.24	353	30.8	37	36.6	0.34	335	30.7	55	34.8	0.30
20-24	458	40.1	37	31.1		456	39.9	33	32.7		423	38.8	66	41.8	
25-29	201	17.6	22	18.5		206	18.0	16	15.8		198	18.2	24	15.2	
>=30	130	11.4	18	15.1		132	11.5	15	14.9		134	12.3	13	8.2	
Pre-Pregnancy BMI															
less than 18.5	69	6.1	10	8.6	0.33	68	6.0	9	9.0	0.11	60	5.6	17	10.8	0.02
18.5-<25.0	549	48.4	52	44.4		538	47.3	56	56.0		513	47.5	81	51.6	
25.0-<30.0	258	22.8	33	28.2		269	23.6	20	20.0		257	23.8	32	20.4	
30 or greater	258	22.8	22	18.8		263	23.1	15	15.0		251	23.2	27	17.2	
Education															
Less than high school	528	48.6	55	50.9	0.39	529	48.5	46	50.6	0.12	487	47.1	88	59.9	0.01
High school graduate or GED	350	32.2	38	35.2		350	32.1	35	38.5		348	33.6	37	25.2	
Post high school	209	19.2	15	13.9		212	19.4	10	11.0		200	19.3	22	15.0	
Income															
less than $15,000	330	30.7	27	25.0	0.53	332	30.7	22	24.4	0.17	309	30.2	45	30.8	0.38
$15,000-$30,000	166	15.4	16	14.8		168	15.5	12	13.3		160	15.6	20	13.7	
$30,000 or greater	69	6.4	6	5.6		71	6.6	3	3.3		69	6.7	5	3.4	
Don't Know/Refused	511	47.5	59	54.6		510	47.2	53	58.9		487	47.5	76	52.1	
Parity															
0 live births	473	41.5	52	43.7	0.56	468	40.9	49	48.5	0.33	432	39.7	85	53.8	<0.01
1 live birth	351	30.8	31	26.1		353	30.9	27	26.7		342	31.5	38	24.1	
2 or more live births	316	27.7	36	30.3		323	28.2	25	24.8		313	28.8	35	22.2	
History of Preterm Delivery															
no	1027	91.5	91	77.8	<0.01	1025	91.1	81	80.2	<0.01	n/a		n/a		
yes	95	8.5	26	22.2		100	8.9	20	19.8		n/a		n/a		
History of IUGR															
no	n/a		n/a			1089	99.7	97	99.0	0.29*	1036	99.7	150	99.3	0.42*
yes	n/a		n/a			3	0.3	1	1.0		3	0.3	1	0.7	
Acculturation															
Low	817	78.7	80	84.2	0.21	824	79.0	64	81.0	0.67	779	79.2	109	79.0	0.96
High	221	21.3	15	15.8		219	21.0	15	19.0		205	20.8	29	21.0	
Generation in U.S.															
Born in PR/DR	513	46.3	60	52.6	0.41	519	46.7	47	48.0	0.50	497	47.1	69	44.8	0.80
Parent born in PR/DR	529	47.8	49	43.0		527	47.4	48	49.0		498	47.2	77	50.0	
Grandparent born in PR/DR	65	5.9	5	4.4		66	5.9	3	3.1		61	5.8	8	5.2	
Live with partner/spouse															
no	527	49.1	48	44.9	0.41	525	48.7	45	50.0	0.81	498	48.7	72	49.3	0.89
yes	547	50.9	59	55.1		554	51.3	45	50.0		525	51.3	74	50.7	
Trait Anxiety															
1st quartile	295	27.8	32	31.4	0.46	298	27.9	25	30.1	0.72	284	28.0	39	37.9	0.47
2nd quartile	257	24.2	26	25.5		259	24.2	20	24.1		245	24.2	34	24.3	
3rd quartile	249	23.4	26	25.5		250	23.4	22	26.5		245	24.2	27	19.3	
4th quartile	262	24.7	18	17.7		263	24.6	16	19.3		239	23.6	40	28.6	
Pre-Pregnancy															
Smoking															
no	736	67.7	68	62.6	0.33	738	67.5	56	62.9	0.38	709	68.4	85	58.2	0.01
yes	352	32.4	40	37.4		356	32.5	33	37.1		328	31.6	61	41.8	
Alcohol															
no	657	60.3	63	59.4	0.87	658	60.1	53	60.2	0.98	627	60.5	84	57.5	0.50
yes	433	39.7	43	40.6		437	39.9	35	39.8		410	39.5	62	42.5	
Early Pregnancy															
Smoking															
no	650	86.4	72	81.8	0.24	660	86.1	54	84.4	0.71	640	87.2	74	76.3	<0.01
yes	102	13.6	16	18.2		107	14.0	10	15.6		94	12.8	23	23.7	
Alcohol															
no	735	97.6	84	95.4	0.28*	748	97.4	62	96.9	0.68*	714	97.1	96	99.0	0.50*
yes	18	2.4	4	4.6		20	2.6	2	3.1		21	2.9	1	1.0	
Stress															
1st quartile	230	30.6	31	36.1	0.59	241	31.5	19	31.2	0.46	234	31.9	25	26.3	0.63
2nd quartile	166	22.1	20	23.3		162	21.2	18	29.5		157	21.4	24	25.3	
3rd quartile	184	24.5	16	18.6		185	24.2	12	19.7		173	23.6	25	26.3	
4th quartile	172	22.9	19	22.1		177	23.1	12	19.7		170	23.2	21	22.1	
Mid-Pregnancy															
Smoking															
no	626	88.5	54	77.1	<0.01	632	88.5	43	76.8	0.01	596	87.9	79	85.9	0.58
yes	81	11.5	16	22.9		82	11.5	13	23.2		82	12.1	13	14.1	

Table 2.5 Distribution of covariates by birth outcomes in the study population: Proyecto Buena Salud, 2006-2011 (continued)

		Preterm Birth (n=1262)					Low Birth Weight (n=1248)					Small for Gestational Age (n=1248)				
		No		Yes			No		Yes			No		Yes		
		n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
Alcohol																
	no	698	99.0	69	98.6	0.54*	704	98.9	56	100.0	1.00*	668	98.8	92	100.0	0.61*
	yes	7	1.0	1	1.4		8	1.1	0	0.0		8	1.2	0	0.0	
Stress																
	1st quartile	196	27.8	13	18.6	0.33	201	28.1	9	16.4	0.11	182	26.8	25	27.5	0.87
	2nd quartile	177	25.1	17	24.3		177	24.8	11	20.0		169	24.9	20	22.0	
	3rd quartile	167	23.7	21	30.0		171	23.9	17	30.9		163	24.0	25	27.5	
	4th quartile	166	23.5	19	27.1		166	23.2	18	32.7		164	24.2	21	23.1	
State Anxiety																
	1st quartile	160	29.3	17	27.4	0.91	164	29.2	11	26.8	0.98	153	28.6	22	32.8	0.84
	2nd quartile	111	20.3	15	24.2		115	20.5	8	19.5		110	20.6	13	19.4	
	3rd quartile	142	26.0	16	25.8		146	26.0	11	26.8		142	26.5	15	22.4	
	4th quartile	133	24.4	14	22.6		136	24.2	11	26.8		130	24.3	17	25.4	
Late Pregnancy																
Smoking																
	no	637	89.0	41	87.2	0.72	634	89.4	37	78.7	0.02	596	89.9	75	80.7	<0.01
	yes	79	11.0	6	12.8		75	10.6	10	21.3		67	10.1	18	19.4	
Alcohol																
	no	708	98.9	45	95.7	0.12*	700	98.7	46	97.9	0.48*	655	98.8	91	97.9	0.35*
	yes	8	1.1	2	4.3		9	1.3	1	2.1		8	1.2	2	2.1	
Stress																
	1st quartile	182	35.5	13	27.7	0.91	176	24.9	15	31.9	0.34	166	25.1	27	29.0	0.14
	2nd quartile	189	26.4	11	23.4		188	26.6	7	14.9		179	27.0	19	20.4	
	3rd quartile	170	23.8	10	21.3		167	23.6	12	25.5		160	24.2	17	18.3	
	4th quartile	174	24.3	13	27.7		176	24.9	13	27.7		157	23.7	30	32.3	
State Anxiety																
	1st quartile	181	25.4	14	29.8	0.85	177	25.1	14	29.8	0.22	169	25.6	22	23.7	0.04
	2nd quartile	188	26.4	10	21.3		184	26.1	13	27.7		170	25.8	27	29.0	
	3rd quartile	178	25.0	12	25.5		184	26.1	6	12.8		176	26.7	14	15.1	
	4th quartile	166	23.3	11	23.4		161	22.8	14	29.8		145	22.0	30	32.3	

* Fisher's Exact Test

Table 2.6 Odds ratios of preterm birth by depression: Proyecto Buena Salud, 2006-2011

		Preterm Birth		Unadjusted		Adjusted Model 1		Adjusted Model 2		Adjusted Model 3		Adjusted Model 4	
		n	%	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Early Pregnancy*													
Depressive symptoms- continuous				0.98	0.94, 1.02	1.00	0.95, 1.04	1.00	0.95, 1.04	1.02	0.95, 1.09	1.02	0.95, 1.09
Any probable depression													
	no	68	11.2	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	20	8.5	0.74	0.44, 1.24	0.68	0.38, 1.22	0.68	0.38, 1.22	0.99	0.47, 2.08	0.99	0.47, 2.08
Probable major depression													
	no	77	11.1	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	11	7.2	0.64	0.32,1.21	0.55	0.35, 1.19	0.55	0.35, 1.19	0.83	0.33, 2.08	0.83	0.33, 2.08
Mid Pregnancy **													
Depressive symptoms- continuous				1.00	0.96, 1.04	1.00	0.95, 1.04	0.99	0.95, 1.03	1.00	0.95, 1.06	1.00	0.94, 1.05
Any probable depression													
	no	53	9.0	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	17	8.8	0.97	0.55, 1.72	0.91	0.50, 1.68	0.82	0.44, 1.52	0.98	0.49, 1.96	0.91	0.45, 1.85
Probable major depression													
	no	59	9.3	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	11	7.6	0.80	0.41, 1.57	0.86	0.43, 1.73	0.74	0.36, 1.52	0.88	0.41, 1.91	0.79	0.36, 1.73

*Early Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity, history of PTB, acculturation
Model 2- same as model 1
Model 3- maternal age, pre-pregnancy BMI, parity, history of PTB, acculturation, trait anxiety
Model 4 - same as model 3

**Mid Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity, history of PTB, generation in U.S.
Model 2- maternal age, pre-pregnancy BMI,parity, history of PTB, generation in U.S., mid-pregnancy smoking
Model 3- maternal age, pre-pregnancy BMI, parity, history of PTB, generation in U.S., mid-pregnancy state anxiety
Model 4- maternal age, pre-pregnancy BMI, parity, history of PTB, generation in U.S., mid-pregnancy smoking, mid-pregnancy state anxiety

Table 2.7 Odds ratios of low birth weight by depression: Proyecto Buena Salud, 2006-2011

		Low Birth Weight		Unadjusted		Adjusted Model 1		Adjusted Model 2		Adjusted Model 3		Adjusted Model 4	
		n	%	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Early Pregnancy*													
Depressive symptoms- continuous				0.97	0.93, 1.01	0.98	0.93, 1.03	0.98	0.93, 1.03	1.02	0.95, 1.10	1.02	0.95, 1.10
Any probable depression													
	no	50	8.3	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	14	6.0	0.71	0.38, 1.31	0.73	0.38, 1.41	0.73	0.38, 1.41	1.11	0.49, 2.55	1.11	0.49, 2.55
Probable major depression													
	no	55	8.0	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	9	6.0	0.73	0.35, 1.52	0.78	0.36, 1.70	0.78	0.36, 1.70	1.38	0.52, 3.69	1.38	0.52, 3.69
Mid Pregnancy**													
Depressive symptoms- continuous				1.03	0.99, 1.08	1.03	0.99, 1.08	1.02	0.98, 1.07	1.02	0.98, 1.07	1.02	0.98, 1.07
Any probable depression													
	no	38	6.5	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	18	9.3	1.47	0.82, 2.64	1.53	0.84, 2.77	1.36	0.74, 2.51	1.36	0.74, 2.51	1.36	0.74, 2.51
Probable major depression													
	no	44	7.0	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	12	8.3	1.21	0.62, 2.36	1.21	0.62, 2.38	1.05	0.53, 2.10	1.05	0.53, 2.10	1.05	0.53, 2.10
Late Pregnancy**													
Depressive symptoms- continuous				1.01	0.96, 1.06	1.00	0.95, 1.06	0.99	0.94, 1.04	0.99	0.94, 1.04	0.99	0.94, 1.04
Any probable depression													
	no	36	5.9	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	11	7.4	1.28	0.63, 2.58	1.18	0.58, 2.39	1.00	0.47, 2.13	1.00	0.47, 2.13	1.00	0.47, 2.13
Probable major depression													
	no	38	5.8	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	9	9.2	1.65	0.77, 3.53	1.52	0.70, 3.30	1.20	0.52, 2.77	1.20	0.52, 2.77	1.20	0.52, 2.77

*Early Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity, acculturation
Model 2- same as Model 1
Model 3- maternal age, pre-pregnancy BMI, parity, acculturation, trait anxiety
Model 4- same as Model 3

**Mid Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity
Model 2-maternal age, pre-pregnancy BMI, parity, mid-pregnancy smoking
Model 3- same as Model 2
Model 4- same as model 2

***Late Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity
Model 2-maternal age, pre-pregnancy BMI, parity, pre-pregnancy smoking, late pregnancy smoking
Model 3- same as model 2
Model 4- same as Model 2

Table 2.8 Odds ratios of small-for-gestational age by depression: Proyecto Buena Salud, 2006-2011

		Small-for-Gestational Age		Unadjusted		Adjusted Model 1		Adjusted Model 2		Adjusted Model 3		Adjusted Model 4	
		n	%	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI	OR	95%CI
Early Pregnancy													
Depressive symptoms- continuous				1.02	0.98, 1.05	1.02	0.99, 1.06	1.02	0.99, 1.06	1.05	1.00, 1.11	1.05	1.00, 1.11
Any probable depression													
	no	66	11.0	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	32	13.7	1.30	0.82, 2.04	1.45	0.91, 2.30	1.45	0.91, 2.30	1.78	0.90, 3.52	1.78	0.90, 3.52
Probable major depression													
	no	75	10.9	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	23	15.3	1.48	0.89, 2.44	1.56	0.93, 2.61	1.56	0.93, 2.61	1.71	0.85, 3.46	1.71	0.85, 3.46
Mid Pregnancy													
Depressive symptoms- continuous				1.03	0.99, 1.06	1.03	1.00, 1.07	1.03	1.00, 1.07	1.04	1.00, 1.09	1.04	1.00, 1.09
Any probable depression													
	no	64	11.0	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	29	15.0	1.43	0.89, 2.29	1.66	1.02, 2.70	1.66	1.02, 2.70	1.77	1.02, 3.07	1.77	1.02, 3.07
Probable major depression													
	no	70	11.1	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	23	16.0	1.52	0.91, 2.53	1.72	1.02, 2.90	1.72	1.02, 2.90	1.82	1.01, 3.25	1.82	1.01, 3.25
Late Pregnancy													
Depressive symptoms- continuous				1.03	0.99, 1.06	1.03	0.99, 1.07	1.02	0.98, 1.06	1.02	0.97, 1.07	1.01	0.96, 1.06
Any probable depression													
	no	71	11.7	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	22	14.9	1.32	0.79, 2.22	1.29	0.76, 2.19	1.17	0.67, 2.04	1.01	0.53, 1.92	0.92	0.47, 1.82
Probable major depression													
	no	77	11.7	1.00	ref	1.00	ref	1.00	ref	1.00	ref	1.00	ref
	yes	16	16.3	1.48	0.82, 2.65	1.48	0.81, 2.71	1.25	0.65, 2.37	1.17	0.58, 2.36	0.99	0.47, 2.09

*Early Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity
Model 2- same as model 2
Model 3- maternal age, pre-pregnancy BMI, parity, trait anxiety
Model 4- same as Model 3

**Mid Pregnancy
Model 1-maternal age, pre-pregnancy BMI, parity
Model 2- same as model 2
Model 3- maternal age, pre-pregnancy BMI, parity, mid-pregnancy state anxiety
Model4- same as Model 3

***Late Pregnancy
Model 1- maternal age, pre-pregnancy BMI, parity
Model 2-maternal age, pre-pregnancy BMI, parity, pre-pregnancy smoking, late pregnancy smoking
Model 3- maternal age, pre-pregnancy BMI, parity, pre-pregnancy smoking, late pregnancy smoking, late pregnancy state anxiety
Model 4- same as Model 3

Table 2.9 Odds ratios of PTB, LBW and SGA by depression among women with no documented antidepressant use or prescriptions during pregnancy: Proyecto Buena Salud, 2006-2011

	Preterm Birth						Low Birth Weight						Small for Gestational Age					
			Unadjusted		Adjusted*				Unadjusted		Adjusted**				Unadjusted		Adjusted**	
	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Early Pregnancy																		
Any probable depression	822						813						813					
no	64	10.8	1.00	ref	1.00	ref	47	8.0	1.00	ref	1.00	ref	62	10.5	1.00	ref	1.00	ref
yes	19	8.4	0.76	0.44, 1.30	0.84	0.48, 1.48	14	6.3	0.77	0.42, 1.43	0.88	0.48, 1.66	32	14.3	1.42	0.90, 2.24	1.54	0.97, 2.47
Probable major depression																		
no	72	10.6	1.00	ref	1.00	ref	52	7.8	1.00	ref	1.00	ref	71	10.6	1.00	ref	1.00	ref
yes	11	7.6	0.70	0.36, 1.35	0.75	0.37, 1.51	9	6.3	0.81	0.39, 1.68	0.90	0.43, 1.89	23	16.2	1.63	0.98, 2.72	1.68	1.00, 2.83
Mid Pregnancy																		
Any probable depression	747						740						740					
no	49	8.5	1.00	ref	1.00	ref	36	6.3	1.00	ref	1.00	ref	63	11.1	1.00	ref	1.00	ref
yes	15	8.8	1.03	0.57, 1.90	0.97	0.52, 1.81	17	10.0	1.65	0.90, 3.12	1.74	0.94, 3.22	27	15.9	1.52	0.93, 2.47	1.76	1.07, 2.91
Probable major depression																		
no	54	8.7	1.00	ref	1.00	ref	41	6.7	1.00	ref	1.00	ref	68	11.0	1.00	ref	1.00	ref
yes	10	8.0	0.92	0.45, 1.85	0.88	0.42, 1.81	12	9.7	1.50	0.77, 2.95	1.52	0.77, 3.01	22	17.7	1.74	1.03, 2.94	1.96	1.14, 3.36
Late Pregnancy																		
Any probable depression							733						733					
no	n/a	n/a	n/a	n/a	n/a	n/a	34	5.7	1.00	ref	1.00	ref	69	11.6	1.00	ref	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	n/a	11	7.9	1.40	0.69, 2.84	1.27	0.62, 2.60	22	15.7	1.42	0.84, 2.38	1.37	0.81, 2.34
Probable major depression																		
no	n/a	n/a	n/a	n/a	n/a	n/a	36	5.6	1.00	ref	1.00	ref	75	11.7	1.00	ref	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	n/a	9	9.8	1.82	0.85, 3.92	1.61	0.74, 3.54	16	17.4	1.59	0.88, 2.87	1.57	0.85, 2.89

*Adjusted for age, BMI, parity, history of preterm birth

** Adjusted for age, BMI, parity

Table 2.10 Odds ratios of PTB, LBW and SGA by depression stratified by stress and anxiety: Proyecto Buena Salud, 2006-2011

	Preterm Birth					Low Birth Weight					Small for Gestational Age				
	n			Unadjusted		n			Unadjusted		n			Unadjusted	
	Total	PTB	%	OR	95%CI	Total	LBW	%	OR	95%CI	Total	SGA	%	OR	95%CI
Stress															
Early Pregnancy															
Low Stress															
Any probable depression															
no	537	58	10.8	1.00	ref	531	43	8.1	1.00	ref	531	58	10.9	1.00	ref
yes	110	9	8.2	0.74	0.35, 1.53	107	7	6.5	0.79	0.35, 1.82	107	16	15.0	1.49	0.79, 2.61
Probable major depression															
no	589	63	10.7	1.00	ref	582	47	8.1	1.00	ref	582	64	11.0	1.00	ref
yes	58	4	6.9	0.62	0.22, 1.77	56	3	5.4	0.64	0.19, 2.14	56	10	17.9	1.76	0.85, 3.66
High Stress															
Any probable depression															
no	66	8	12.1	1.00	ref	66	5	7.6	1.00	ref	66	5	7.6	1.00	ref
yes	125	11	8.8	0.70	0.27, 1.83	125	7	5.6	0.72	0.22, 2.38	125	16	12.8	1.79	0.63, 5.13
Probable major depression															
no	98	12	12.2	1.00	ref	98	6	6.1	1.00	ref	98	8	8.2	1.00	ref
yes	93	7	7.5	0.58	0.22, 1.55	93	6	6.5	1.06	0.33, 3.40	93	13	14.0	1.83	0.72, 4.64
Mid Pregnancy															
Low Stress															
Any probable depression															
no	514	44	8.6	1.00	ref	508	32	6.3	1.00	ref	509	57	11.2	1.00	ref
yes	77	7	9.1	1.07	0.46, 2.47	76	5	6.6	1.05	0.40, 2.78	77	13	17.1	1.63	0.85, 3.15
Probable major depression															
no	546	48	8.8	1.00	ref	540	34	6.3	1.00	ref	540	61	11.3	1.00	ref
yes	45	3	6.7	0.74	0.22, 2.48	44	3	6.8	1.09	0.32, 3.70	44	9	20.5	2.02	0.93, 4.40
High Stress															
Any probable depression															
no	71	9	12.7	1.00	ref	71	6	8.5	1.00	ref	71	6	8.5	1.00	ref
yes	114	10	8.8	0.66	0.26, 1.72	114	12	10.5	1.27	0.46, 3.56	114	15	13.2	1.64	0.61, 4.45
Probable major depression															
no	87	11	12.6	1.00	ref	87	9	10.3	1.00	ref	87	7	8.1	1.00	ref
yes	98	8	8.2	0.61	0.24, 1.61	98	9	9.2	0.88	0.33, 2.32	98	14	14.3	1.91	0.73, 4.96
Late Pregnancy															
Low Stress															
Any probable depression															
no	n/a	n/a	n/a	n/a	n/a	524	32	6.1	1.00	ref	524	58	11.1	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	44	2	4.6	0.73	0.17, 3.16	44	5	11.4	1.03	0.39, 2.72
Probable major depression															
no	n/a	n/a	n/a	n/a	n/a	546	33	6.0	1.00	ref	546	61	11.2	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	22	1	4.6	0.74	0.10, 5.68	22	2	9.1	0.80	0.18, 3.49
High Stress															
Any probable depression															
no	n/a	n/a	n/a	n/a	n/a	83	4	4.8	1.00	ref	83	13	15.7	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	104	9	8.7	1.87	0.56, 6.31	104	17	16.4	1.05	0.48, 2.31
Probable major depression															
no	n/a	n/a	n/a	n/a	n/a	111	5	4.5	1.00	ref	111	16	14.4	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	76	8	10.5	2.49	0.78, 7.94	76	14	18.4	1.34	0.61, 2.94
Anxiety															
Early Pregnancy															
Not High Trait Anxiety															
Any probable depression															
no	552	64	11.6	1.00	ref	546	47	8.6	1.00	ref	546	60	11.0	1.00	ref
yes	74	10	13.5	1.12	0.58, 2.44	72	7	9.7	1.14	0.50, 2.64	72	10	13.9	1.31	0.64, 2.68
Probable major depression															
no	593	69	11.6	1.00	ref	586	51	8.7	1.00	ref	586	65	11.1	1.00	ref
yes	33	5	15.2	1.36	0.51, 3.63	32	3	9.4	1.09	0.32, 3.69	32	5	15.6	1.48	0.55, 3.99
High Trait Anxiety															
Any probable depression															
no	54	3	5.6	1.00	ref	54	2	3.7	1.00	ref	54	5	9.3	1.00	ref
yes	160	10	6.3	1.13	0.30, 4.28	159	7	4.4	1.20	0.24, 5.95	159	22	13.8	1.57	0.57, 4.38
Probable major depression															
no	97	7	7.2	1.00	ref	97	3	3.1	1.00	ref	97	9	9.3	1.00	ref
yes	117	6	5.1	0.70	0.23, 2.14	116	6	5.2	1.71	0.42, 7.02	116	18	15.5	1.80	0.77, 4.20

Table 2.10 Odds ratios of PTB, LBW and SGA by depression stratified by stress and anxiety: Proyecto Buena Salud, 2006-2011 (continued)

	Preterm Birth					Low Birth Weight					Small for Gestational Age				
	n			Unadjusted		n			Unadjusted		n			Unadjusted	
	Total	PTB	%	OR	95%CI	Total	LBW	%	OR	95%CI	Total	SGA	%	OR	95%CI
Mid Pregnancy															
Not High State Anxiety															
Any probable depression															
no	408	42	10.3	1.00	ref	403	25	6.2	1.00	ref	403	44	10.9	1.00	ref
yes	53	6	11.3	1.11	0.45, 2.76	52	5	9.6	1.61	0.59, 4.40	52	6	11.5	1.06	0.43, 2.64
Probable major depression															
no	425	46	10.8	1.00	ref	420	28	6.7	1.00	ref	420	46	11.0	1.00	ref
yes	36	2	5.6	0.49	0.11, 2.08	35	2	5.7	0.85	0.19, 3.72	35	4	11.4	1.05	0.35, 3.11
High State Anxiety															
Any probable depression															
no	58	6	10.3	1.00	ref	58	4	6.9	1.00	ref	58	6	10.3	1.00	ref
yes	89	8	9.0	0.86	0.28, 2.61	89	7	7.9	1.15	0.32, 4.13	89	11	12.4	1.22	0.43, 3.51
Probable major depression															
no	75	8	10.7	1.00	ref	75	6	8.0	1.00	ref	75	7	9.3	1.00	ref
yes	72	6	8.3	0.76	0.25, 2.31	72	5	6.9	0.86	0.25, 2.95	72	10	13.9	1.57	0.56, 4.37
Late Pregnancy															
Not High State Anxiety															
Any probable depression															
no	n/a	n/a	n/a	n/a	n/a	529	33	6.2	1.00	ref	529	60	11.3	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	49	0	0	#		49	3	6.1	0.51	0.15, 1.69
Probable major depression															
no	n/a	n/a	n/a	n/a	n/a	554	33	6.0	1.00	ref	554	62	11.2	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	24	0	0	#		24	1	4.2	0.35	0.05, 2.60
High State Anxiety															
Any probable depression															
no	n/a	n/a	n/a	n/a	n/a	76	3	4.0	1.00	ref	76	11	14.5	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	99	11	11	3.04	0.82, 11.31	99	19	19.2	1.40	0.62, 3.16
Probable major depression															
no	n/a	n/a	n/a	n/a	n/a	101	5	5.0	1.00	ref	101	15	14.9	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	74	9	12	2.66	0.85, 8.29	74	15	20.3	1.46	0.66, 3.21

Model unable to run

Table 2.11 Odds ratios of PTB, LBW, and SGA by composite variables of depression with stress and anxiety: Proyecto Buena Salud, 2006-2011

	Preterm Birth						Low Birth Weight						SGA					
			Unadjusted		Adjusted*				Unadjusted		Adjusted**				Unadjusted		Adjusted**	
	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Depression and Stress																		
Early Pregnancy																		
no major depression/not high stress	63	10.7	1.00	ref	1.00	ref	47	8.1	1.00	ref	1.00	ref	64	11.0	1.00	ref	1.00	ref
no major depression/high stress	12	12.2	1.17	0.60, 2.25	1.22	0.61, 1.92	6	6.1	0.74	0.31, 1.79	0.79	0.33, 1.92	8	8.2	0.72	0.33, 1.55	0.73	0.34, 1.58
major depression/not high stress	4	6.9	0.62	0.22, 1.77	0.52	0.16, 1.77	3	5.4	0.64	0.19, 2.14	0.73	0.22, 2.46	10	17.9	1.76	0.85, 3.66	1.94	0.92, 4.11
major depression/high stress	7	8.1	0.68	0.30, 1.53	0.83	0.36, 1.92	6	6.5	0.79	0.33, 1.89	0.90	0.37, 2.20	13	14.0	1.32	0.69, 2.50	1.32	0.69, 2.53
Mid Pregnancy																		
no major depression/not high stress	48	8.8	1.00	ref	1.00	ref	34	6.3	1.00	ref	1.00	ref	61	11.3	1.00	ref	1.00	ref
no major depression/high stress	11	12.9	1.50	0.75, 3.02	1.90	0.92, 3.94	9	10.3	1.72	0.79, 3.72	1.89	0.86, 4.16	7	8.1	0.69	0.30, 1.56	0.68	0.30, 1.55
major depression/not high stress	3	6.7	0.74	0.22, 2.48	0.61	0.17, 2.16	3	6.8	1.09	0.32, 3.70	1.07	0.31, 3.67	9	20.5	2.02	0.93, 4.40	2.18	0.98, 4.84
major depression/high stress	8	8.2	0.92	0.42, 2.02	0.99	0.44, 2.22	9	9.2	1.51	0.70, 3.25	1.55	0.71, 3.37	14	14.3	1.31	0.70, 2.45	1.50	0.79, 2.85
Late Pregnancy																		
no major depression/not high stress	n/a	n/a	n/a	n/a	n/a	n/a	33	6.0	1.00	ref	1.00	ref	61	11.2	1.00	ref	1.00	ref
no major depression/high stress	n/a	n/a	n/a	n/a	n/a	n/a	5	5.0	0.73	0.28, 1.92	0.72	0.27, 1.91	16	14.4	1.34	0.74, 2.42	1.41	0.77, 2.58
major depression/not high stress	n/a	n/a	n/a	n/a	n/a	n/a	0	0	0.74	0.10, 5.67	0.64	0.08, 5.01	2	9.1	0.80	0.18, 3.49	0.79	0.18, 3.53
major depression/high stress	n/a	n/a	n/a	n/a	n/a	n/a	9	12.2	1.83	0.81, 4.12	1.71	0.74, 3.93	14	18.4	1.80	0.95, 3.40	1.83	0.94, 3.55
Depression and Anxiety																		
Early Pregnancy																		
no major depresion/not high trait anxiety	69	11.6	1.00	ref	1.00	ref	51	8.7	1.00	ref	1.00	ref	65	11.1	1.00	ref	1.00	ref
no major depression/high trait anxiety	7	8.1	0.59	0.26, 1.33	0.68	0.30, 1.55	3	3.1	0.34	0.10, 1.10	0.37	0.11, 1.24	9	9.3	0.82	0.84, 2.59	0.93	0.44, 1.96
major depression/not high trait anxiety	5	15.2	1.36	0.51, 3.63	1.47	0.48, 4.47	3	9.4	1.09	0.32, 3.69	1.23	0.35, 4.31	5	15.6	1.48	0.55, 3.99	1.45	0.53, 4.00
major depression/high trait anxiety	6	5.1	0.41	0.17, 0.97	0.48	0.20, 1.15	6	5.2	0.57	0.24, 1.37	0.67	0.28, 1.61	18	15.5	1.47	0.84, 2.59	1.62	0.91, 2.88
Mid Pregnancy																		
no major depresion/not high state anxiety	46	10.8	1.00	ref	1.00	ref	28	6.7	1.00	ref	1.00	ref	46	11.0	1.00	ref	1.00	ref
no major depression/high state anxiety	8	10.7	0.98	0.44, 2.18	0.91	0.40, 2.11	6	8.0	1.22	0.49, 3.05	1.26	0.50, 3.21	7	9.3	0.84	0.36, 1.93	0.84	0.36, 1.95
major depression/not high state anxiety	2	5.6	0.49	0.11, 2.08	0.39	0.09, 1.75	2	5.7	0.85	0.19, 3.72	0.89	0.20, 3.96	4	11.4	1.05	0.35, 3.11	1.08	0.36, 3.25
major depression/high state anxiety	6	8.3	0.75	0.31, 1.82	0.74	0.29, 1.88	5	6.9	1.05	0.39, 2.80	1.03	0.38, 2.81	10	13.9	1.31	0.63, 2.74	1.54	0.72, 3.29
Late Pregnancy																		
no major depresion/not high state anxiety	n/a	n/a	n/a	n/a	n/a	n/a	33	6.0	1.00	ref	1.00	ref	62	11.2	1.00	ref	1.00	ref
no major depression/high state anxiety	n/a	n/a	n/a	n/a	n/a	n/a	5	4.9	#		#		15	14.9	1.38	0.75, 2.54	1.38	0.75, 2.56
major depression/not high state anxiety	n/a	n/a	n/a	n/a	n/a	n/a	0	0.0	#		#		1	4.2	0.35	0.05, 2.60	0.32	0.04, 2.48
major depression/high state anxiety	n/a	n/a	n/a	n/a	n/a	n/a	9	12.3	#		#		15	20.3	2.02	1.08, 3.77	2.08	1.08, 3.98

* Adjusted for age, pre-pregnancy BMI, parity, history of preterm birth

** Adjusted for age, pre-pregnancy BMI, parity

[#]Model unable to run

Table 2.12 Odds ratios of PTB, LBW and SGA by patterns of depressive symptoms and depression during pregnancy: Proyecto Buena Salud, 2006-2011

	Preterm Birth*								Low Birth Weight**								Small for Gestational Age**							
			Unadjusted		Adjusted		Adjusted***				Unadjusted		Adjusted		Adjusted***				Unadjusted		Adjusted		Adjusted***	
	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI
Change in EPDS Score - Early to Mid Pregnancy																								
EPDS score -continuous Increase in Depressive Symptoms			1.00	0.94, 1.06	0.98	0.92, 1.04	0.96	0.89, 1.03			1.07	0.99, 1.15	1.06	0.99, 1.15	1.05	0.97,1.14			1.02	0.97, 1.08	1.02	0.97, 1.08	1.03	0.97, 1.09
no	27	9.1	1.00	ref	1.00	ref	1.00	ref	14	4.8	1.00	ref	1.00	ref	1.00	ref	29	9.8	1.00	ref	1.00	ref	1.00	ref
yes	20	10.9	1.22	0.66, 2.25	1.00	0.52, 1.94	0.95	0.48, 1.90	15	8.3	1.83	0.86, 3.88	1.63	0.76, 3.52	1.47	0.66, 3.26	22	12.2	1.28	0.71, 2.3	1.27	0.69, 2.32	1.31	0.70, 2.44
Change in EPDS Score - Mid to Late Pregnancy																								
EPDS score -continuous Increase in Depressive Symptoms	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a			1.01	0.93,1.101	1.01	0.93, 1.10	1.05	0.96, 1.15			1.00	0.95, 1.06	1.01	0.95, 1.07	1.04	0.97,1.11
no	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	13	5.4	1.00	ref	1.00	ref	1.00	ref	29	12.0	1.00	ref	1.00	ref	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	7	5.0	0.92	0.36, 2.36	0.95	0.36, 2.50	1.16	0.41,3.28	15	10.6	0.87	0.45, 1.69	0.91	0.45, 1.81	1.09	0.52, 5.36
Change in EPDS Score - Early to Late Pregnancy																								
EPDS score -continuous Increase in Depressive Symptoms	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a			1.01	0.94, 1.08	1.00	0.93, 1.07	1.00	0.92,1.09			1.02	0.97, 1.07	1.02	0.97, 1.08	1.04	0.98, 1.10
no	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	18	5.7	1.00	ref	1.00	ref	1.00	ref	34	10.8	1.00	ref	1.00	ref	1.00	ref
yes	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	10	6.0	1.05	0.48, 2.34	0.88	0.39, 1.99	0.90	0.39,2.10	20	12.0	1.13	0.63, 2.03	1.09	0.60, 2.00	1.19	0.63, 2.23
Duration of Exposure to Probable Major Depression Across Pregnancy																								
Major Depression Across Early and Mid-Pregnancy Periods																								
continuous variable[##]			0.62	0.34, 1.12	0.61	0.34, 1.11					0.98	0.54, 1.78	0.94	0.51, 1.74	n/a	n/a			1.23	0.80, 1.88	1.30	0.84, 2.03	n/a	n/a
categorical variable																								
none	38	10.9	1.00	ref	1.00	ref	n/a	n/a	22	6.3	1.00	ref	1.00	ref	n/a	n/a	34	9.8	1.00	ref	1.00	ref	n/a	n/a
one pregnancy period	8	9.0	0.81	0.36, 1.81	1.06	0.45, 2.47	n/a	n/a	4	4.6	0.70	0.24, 2.10	0.65	0.22, 1.98	n/a	n/a	12	13.6	1.45	0.72, 2.94	1.51	0.73, 3.10	n/a	n/a
both pregnancy periods	1	2.5	0.21	0.03, 1.58	0.15	0.02, 1.17	n/a	n/a	3	7.5	1.20	0.34, 4.19	1.15	0.32, 4.11	n/a	n/a	5	12.5	1.32	0.48, 3.58	1.52	0.54, 4.23	n/a	n/a
Major Depression Across Mid and Late Pregnancy Periods																								
continuous variable[##]			n/a	n/a	n/a	n/a					1.85	1.00, 3.43	1.74	0.91, 3.32					1.48	0.92, 2.38	1.66	1.00, 2.74		
categorical variable																								
none	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	13	4.4	1.00	ref	1.00	ref	n/a	n/a	30	10.2	1.00	ref	1.00	ref	n/a	n/a
one pregnancy period	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3	4.6	1.03	0.28, 3.71	0.96	0.36, 3.59	n/a	n/a	9	13.6	1.38	0.62, 3.08	1.59	0.68, 3.73	n/a	n/a
both pregnancy periods	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	4	16.7	4.31	1.29, 14.43	3.85	1.07, 13.86	n/a	n/a	5	20.8	2.31	0.80, 6.63	2.82	0.92, 8.61	n/a	n/a
Major Depression Across Early and Late Pregnancy Periods																								
continuous variable[##]			n/a	n/a	n/a	n/a					1.14	0.63, 2.08	1.23	0.66, 2.27	n/a	n/a			1.51	1.00, 2.27	1.59	1.04, 2.44	n/a	n/a
categorical variable																								
none	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	21	5.7	1.00	ref	1.00	ref	n/a	n/a	36	9.7	1.00	ref	1.00	ref	n/a	n/a
one pregnancy period	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	4	5.2	0.91	0.30, 2.73	0.99	0.32, 3.00	n/a	n/a	11	14.3	1.55	0.75, 3.19	1.70	0.80, 3.57	n/a	n/a
both pregnancy periods	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	3	8.3	1.51	0.43, 5.33	1.75	0.46, 6.60	n/a	n/a	7	19.4	2.24	0.92, 5.48	2.43	0.94, 6.26	n/a	n/a

*adjusted for maternal age, pre-pregnancy BMI, and history of preterm birth
**adjusted for maternal age, pre-pregnancy BMI, and parity
***adjusted for EPDS in earlier pregnancy period of change
[#]P-trend=0.03
[##]Odds ratio for each additional pregnancy period of exposure to major depression

Table 2.13 Odds ratios of subtypes of preterm birth by levels of depression: Proyecto Buena Salud, 2006-2011

	Preterm Birth Type								Spontaneous								Preterm Birth Gestational Age							
	Spontaneous				Medically Indicated				Preterm Labor				PPROM				Early (<34 weeks)				Late (34-36 weeks)			
			Unadjusted				Unadjusted				Unadjusted				Unadjusted				Unadjusted				Unadjusted	
	n	%	OR	95%CI	n	%	OR	95%CI	n	%	OR	95%CI	n	%	OR	95%CI	n	%	OR	95% CI	n	%	OR	95%CI
Early Pregnancy																								
Any probable depression																								
no	49	8.3	1.00	ref	18	3.2	1.00	ref	32	5.6	1.00	ref	17	3.1	1.00	ref	24	4.3	1.00	ref	44	7.5	1.00	ref
yes	16	6.9	0.82	0.46, 1.47	4	1.8	0.56	0.19, 1.66	12	5.3	0.94	0.48, 1.86	4	1.8	0.59	0.20, 1.77	4	1.8	0.42	0.14, 1.22	16	6.9	0.91	0.50, 1.65
Probable major depression																								
no	55	8.2	1.00	ref	21	3.3	1.00	ref	35	5.4	1.00	ref	20	3.1	1.00	ref	25	3.9	1.00	ref	52	7.8	1.00	ref
yes	10	6.6	0.79	0.40, 1.60	1	0.7	0.21	0.03, 1.56	9	6.0	1.12	0.53, 2.30	1	0.7	0.22	0.03, 1.64	3	2.1	0.52	0.16, 1.76	8	5.4	0.67	0.31, 1.45
Mid Pregnancy																								
Any probable depression																								
no	39	6.8	1.00	ref	13	2.4	1.00	ref	24	4.3	1.00	ref	15	2.7	1.00	ref	13	2.4	1.00	ref	40	7.0	1.00	ref
yes	15	7.8	1.16	0.63, 2.16	2	1.1	0.46	0.10, 2.08	8	4.3	1.01*	0.44, 2.28	7	3.8	1.41	0.57, 3.51	4	2.2	0.93	0.30, 2.88	13	6.8	0.98	0.51, 1.88
Probable major depression																					575			
no	45	7.2	1.00	ref	13	2.2	1.00	ref	29	4.8	1.00	ref	16	2.7	1.00	ref	16	2.7	1.00	ref	43	6.9	1.00	ref
yes	9	6.3	0.86	0.41, 1.81	2	1.5	0.66	0.15, 2.97	3	2.2	0.45	0.13, 1.48	6	4.3	1.62	0.62, 4.20	1	0.7	0.27	0.04, 2.05	10	6.9	1.00	0.49, 2.04

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CHAPTER 3

PHYSICAL ACTIVITY AND DEPRESSION AMONG PREGNANT HISPANIC WOMEN

Introduction

Depressive disorders affect up to an estimated 18% of women during pregnancy[1] and are reflective of the high rates of depression experienced by women of childbearing age. Risk for prenatal depression varies for women in the United States by race/ethnicity with some studies finding almost double the prevalence among Hispanic women as compared to non-Hispanic White women.[2] Factors that likely contribute to this disparity include economic, acculturation and social (e.g. racism) challenges experienced by Hispanics living in the United States.[3] Among Hispanics, depression rates vary by nativity with the highest lifetime prevalence levels found amongst Puerto Ricans.[4] Some studies have found estimates of probable prenatal depression as high as 33% in a predominantly Puerto Rican population.[5] As depression during pregnancy has been associated with increased risk of poor maternal health outcomes, both during and following pregnancy (e.g. pre-eclampsia, post-partum depression),[6, 7] and birth outcomes (e.g. admission to neonatal nurseries, small-for-gestational age),[8, 9] it is important to identify ways to prevent or reduce prenatal depression among these populations at high risk.

Physical activity has been proposed as a means to both prevent the onset/reoccurrence of depression and reduce depressive symptoms in individuals experiencing a depressive disorder. Depression relapse rates are particularly high during

pregnancy, with some studies finding relapse rates as high as 43%, likely due to a variety of factors, including the decision made by some women or their providers to discontinue maintenance medication due to conflicting findings about the safety of antidepressant use during pregnancy. Given these concerns about antidepressant treatment, physical activity provides an important potential alternative mechanism to prevent and treat antenatal depression. Current U.S. Health and Human Services guidelines recommend that pregnant women engage in at least 150 minutes of moderate intensity aerobic activity per week,[10] though women often do not meet these guidelines.

Much of the research exploring the relationship between physical activity and depression has taken place in non-pregnant populations. However, mechanisms of action are likely similar. Proposed theories focus on neurobiological and psychological pathways.[11] Commonly suggested neurobiological theories propose that physical activity alleviates/prevents depression through the following: (1) increased synaptic transmission in the brain of serotonin, norepinephrine and dopamine; (2) increased hippocampal neurogenesis through the release of B-endorphins, vascular endothelial growth factor, brain-derived neurotrophic factor, or serotonin; (3) decreased cortisol levels; and (4) increased release of B-endorphins producing a sense of euphoria. Psychological theories focus on physical activity leading to an increase in self-efficacy and as a distraction from depressive symptoms and stimuli as potential mediators of decreased depressive symptoms.

A number of epidemiologic studies have examined the relationship between physical activity and depression; however, far fewer have examined this association among pregnant women. Studies conducted in women in the general population have

generally found that physical activity is inversely associated with depression.[12-14] The majority of studies assessing this relationship among pregnant women have examined this association cross-sectionally.[15-20] The few prospective cohort and intervention studies conducted have tended to find a protective effect of exercise on probable depression or depressive symptoms, but most had limitations, including 1) small sample size,[21] and 2) challenges disentangling the effects of exercise versus those of other intervention components (e.g. participating in a group) in the randomized control trial and quasi-experimental study.[22, 23] Other limitations of both the prospective and cross-sectional studies include use of depression assessment instruments designed for use in the general population that are likely to lead to misclassification in pregnant women, use of unvalidated measures of physical activity, and assessment of physical activity and depressive symptoms at one timepoint in pregnancy. In addition, heterogeneous measures of physical activity (e.g. leisure time activity, exercise, total physical activity) and depression measures that examined varying degrees of depression ranging from depressive symptoms to clinical diagnosis were used making it difficult to compare findings. Finally, the studies predominantly focused on White Non-Hispanic women with little research conducted among Hispanic women.

Therefore, this study furthered the prior literature by prospectively and cross-sectionally examining the association between physical activity and prenatal depression among predominantly Puerto Rican pregnant Hispanic women at different timepoints during pregnancy. We used a validated tool, the Pregnancy Physical Activity Questionnaire, to assess physical activity. We assessed depression using the Edinburgh Postnatal Depression Scale, a tool that takes into account somatic depressive symptoms

that are also common symptoms of pregnancy. We also examined the effects of various domains and intensity levels of physical activity on probable depression and depressive symptoms. A number of sociodemographic, acculturation, behavioral and health factors were considered as potential confounders of the association between physical activity and prenatal depression. This study was the first, to our knowledge, to examine this relationship in a Puerto Rican population.

Physiologic Mechanism

Neurobiological Mechanisms

A number of neurobiological mechanisms have been proposed to explain how physical activity may prevent or alleviate depression.[11, 24] One commonly referenced theory suggests that exercise increases monoamine levels. Norepinephrine, serotonin and dopamine are common monoamines found in the brain that are thought to be associated with depression. Current medications used to treat depression focus on increasing synaptic levels and receptor binding of these monoamines, particularly serotonin and norepinephrine, as it is thought that increasing deficient levels characteristic of depressed individuals will improve depression. Experimental animal studies and several human studies have found an increase in these monoamines, their precursors, or their metabolites following exercise, though they have not been entirely consistent.[25] Despite this evidence, recent studies cast doubt on the viability of this theory as they suggest that anti-depressants targeting monoamine function may provide little benefit beyond that of a placebo among many individuals,[26] though this remains highly debated.[27]

Another commonly proposed neurobiological theory suggests that exercise leads to increased hippocampal neurogenesis.[28] As depression has been associated with decreased hippocampal volume, it is theorized that exercise leads to an increase in hippocampal neurogenesis via the release of neurotrophic factors, including vascular endothelial growth factor, brain-derived neurotrophic factor, and insulin-like growth factor 1. Studies in humans and animals have shown that exercise increases levels of these factors.[29] It has also been suggested that exercise improves mood through the hypothalamic-pituitary-adrenal (HPA) axis as studies have found that exercise decreased cortisol levels, which have found to be elevated in some individuals with depression.[30]

Finally, the release of B-endorphins during exercise has been proposed as a potential mechanism of action explaining how exercise alleviates depression.[31] This release of B-endorphins is thought to promote a euphoric state and is thought to be the underlying mechanism for the phenomenon commonly referred to as "runner's high." Studies examining this association have found conflicting results regarding its viability.[11] Those studies providing support for this theory have demonstrated that: (1) exercise for extended periods of time increases B-endorphin levels,[32] and that (2) increased opioid activity in the brain following running correlated with levels of self-reported euphoria.[33]

Psychological Mechanisms

Psychological mechanisms have also been proposed to explain how physical activity may reduce depression. One commonly theorized psychological mechanism suggests that exercise leads to increased self-efficacy, that in turn, leads to positive feelings that have antidepressant effects.[34] Bandura suggests that low self-efficacy in

depressed individuals results in negative self-concept and negative thinking patterns that contribute to feelings of depression.[35] Therefore, mastery skills that are a result of successful exercise behavior enhance self-efficacy, counteracting these negative thinking patterns. Another proposed psychological theory suggests that exercise is a distraction from negative thoughts associated with depression, thus leading to a reduction in depressive symptoms.[34] Likely, the relationship is mediated by a combination of these proposed psychological and neurobiological mechanisms.

Prior Epidemiologic Research

A number of epidemiologic studies examining the relationship between physical activity and depression in the general population suggest that physical activity is associated with decreased risk of depression or depressive symptoms among women.[12-14] However, far fewer studies have examined this relationship during pregnancy. We identified ten studies published in the English language that examined the association between physical activity and depression, or depressive symptoms, during pregnancy[15-23, 36] with all but one focusing on leisure time activity.[36] Four studies[21-23, 36] examined the association between physical activity and depression/depressive symptoms prospectively, including: two cohort studies, one randomized controlled trial (RCT), and one quasi-experimental study. Among the cohort studies, one found an inverse association between moderate/vigorous physical activity and elevated depression symptoms (OR=0.56),[36] whereas, the other found no association.[21] The RCT and quasi-experimental studies found that the physical activity interventions reduced depressive symptoms (mean change in Centers for Epidemiologic Studies depressive symptom score: -4 to -5.4).[22, 23] The

remaining six studies examined this association cross-sectionally with the majority finding a protective effect of physical activity (OR Range=0.51-0.55).[15-20]

In the largest prospective cohort study examining the effects of physical activity on depression during pregnancy, Demissie et al. examined the effects of total and domain-specific moderate-to-vigorous physical activity (MVPA) on elevated levels of depressive symptoms during pregnancy.[36] This was the only study to examine physical activity from a variety of domains, and not just exercise or leisure time activity. The study included 1220 predominantly Caucasian, pregnant women recruited through prenatal clinics. Information on activities in five domains of moderate-to-vigorous physical activity (occupational, recreational, house- hold, child and adult care, and transportation) was collected through structured seven-day recall questionnaires at 17-22 weeks gestational age (GA). Depressive symptoms were assessed at two time points in pregnancy (<20 weeks GA, 24-29 weeks GA) using the Centers for Epidemiological Studies Depression Scale (CES-D), with elevated scores of 17 or greater indicative of a positive screen for depression. As the CES-D was developed for use and validated in the general population, a higher cut point was chosen than what is commonly recommended (16 or higher) to account for somatic depressive symptoms included in the questionnaire that are also common symptoms of pregnancy. Active women with MVPA ≤2.67 hrs/wk at 17-22 weeks GA had almost half the odds of elevated depressive symptoms at 27-30 weeks GA compared to women with no MVPA (OR=0.56, 95% CI=0.38,0.83) after adjusting for elevated depressive symptoms at 17-22 weeks GA and other potential confounders. This effect was attenuated for women with MVPA>2.67 hrs/wk (OR=0.63, 95% CI=0.50,1.07). Women that engaged in adult and childcare MVPA up to

2.25 hrs/wk (OR=1.84, 95%CI=1.08,3.11;) and indoor household MVPA more than one hr/wk (OR=1.63, 95%CI=0.98,2.70) at 17-22 weeks GA had increased odds of elevated depressive symptoms at 27-30 weeks GA in multivariate analysis. There was not a statistically significant association between physical activity and elevated depressive symptoms in any of the other domains.

Symons Downs et al. conducted the only other prospective cohort study that examined the effects of physical activity, specifically exercise behavior, on depression during pregnancy among 230 predominantly Caucasian, pregnant women recruited through an ob/gyn private practice.[21] Information on leisure time exercise behavior (EB) was collected through the Leisure Time Exercise Questionnaire during each trimester. In addition, pre-pregnancy physical activity was collected retrospectively during the first trimester. Depressive symptoms (DS) were also assessed at each trimester using the CES-D. In cross-sectional analysis, exercise behavior was inversely correlated with depressive symptoms (continuous) during the first trimester (r=-0.20; p=<0.01) and third trimester (r=-0.15;p=0.008). In prospective analyses, exercise behavior in the first trimester did not predict exercise behavior in the second trimester after adjusting for depressive symptoms in the previous trimester and body image satisfaction (*B*=-0.10; 95%CI not shown). Similarly, no association was found between exercise in the second trimester and depressive symptoms in the third trimester (*B*=0.03; 95% CI not shown). This study was limited by its small sample size, which likely affected its power to detect effects.

In the only RCT conducted examining this association, Robledo-Colonia et al. assessed the effect of an intervention that included physical activity on depressive

symptoms among 74 women in Colombia.[22] Women were recruited between 16-20 weeks gestation through prenatal services at three hospitals and were randomized to an intervention (n=37) and control group (n=37). The intervention consisted of a three-month program of three 60-minute supervised group classes per week that included: walking, aerobic exercise, stretching and relaxation. The control group did not participate in the group class and continued with normal prenatal care and activities. Depressive symptoms were assessed prior to and following the intervention using the CES-D. On average, women in the intervention group (mean pre-intervention=16, SD=8; mean post-intervention=11, SD=7) reduced their depressive symptom scores by 4 points more than women in the control group (mean pre-intervention=17, SD=7; mean post-intervention=16, SD=8), which was found to be a statistically significant difference. Though the authors state that exercise led to the improvement in depressive symptoms, as the intervention also included non-exercise components and was conducted in a group format, it is not clear if it was the exercise component that led to the decrease in symptoms.

In summary, few studies have examined the effect of physical activity on prenatal depression prospectively.[21-23, 36] Among these studies, limitations included small sample size limiting power, use of an intervention that included non-exercise components making it difficult to ascertain causality, and a quasi-experimental design that did not take into account potential confounding factors. In addition, only two studies adjusted for depression in the prior pregnancy period.[21, 36] The majority conducted cross-sectional analyses, which does not allow one to determine temporality and raises concerns about reverse causality.

In both the prospective and cross-sectional studies, there was variability in the outcome measure, with some studies focusing on depressive symptoms (continuous) and some focusing on probable depression or elevated symptoms indicative of depression. It is important to distinguish these findings as it is possible that there may not be a linear relationship between physical activity and depression, as it has been suggested that physical activity may be more effective at preventing/alleviating symptoms of mild or moderate depression as compared to those of major depression. In addition, all but one study used depression assessment instruments designed for use in the general population. These instruments are subject to nondifferential misclassification of depression as they include questions of somatic depressive symptoms that are also common symptoms of pregnancy. Some of these studies attempted to account for this misclassification through ad hoc methods, such as raising probable depression cut-points.[18, 36] However, as these methods have not been validated, misclassification is still likely. Only one study used an instrument designed to account for somatic depressive symptoms that are also symptoms of pregnancy, the Edinburgh Postnatal Depression Scale.[19] Finally, the majority of studies only measured physical activity and depression at one timepoint in pregnancy, thus, limiting their ability to assess the effect of physical activity on depression over the course of pregnancy.

Additional limitations must also be considered when evaluating the study results, including: (1) use of unvalidated measures of physical activity,[15-19] (2) no consideration of potential confounders,[15, 16, 18-20, 23], and (3) small sample sizes[15, 16, 19-21, 23]. In addition, all but one study examined leisure time or recreational activity. Among the few studies examining domain of physical activity and depression among pregnant women or in the

general population, some have found differences in the association between physical activity and depression with some domains of physical activity, such as household physical activity, either having no association with depression or increasing risk.[36-38] It is important to better understand these differences as the current HHS physical activity guidelines use examples of household/domestic physical activity in their guidance to the public suggesting ways to incorporate moderate physical activity into daily activities. Finally, the majority of the studies were conducted in predominantly White Non-Hispanic populations[15, 16, 20, 21, 36] with few studies including Hispanic women[17, 22, 23] a population at high-risk for depression during pregnancy.

Summary

Depressive disorders are common during pregnancy and have been associated with increased risk of poor maternal and fetal outcomes. Hispanic women are disproportionately affected with some studies finding a prevalence of probable antenatal depression as high as 33%.[5] It is important to identify potential mechanisms to lessen symptoms and prevent the onset or reoccurrence of depression during pregnancy in this high-risk population.

Physical activity is one such mechanism that has been suggested to both prevent depression and reduce depressive symptoms. Several proposed neurobiological and psychological theories have been suggested to explain physical activity's effects that include elevated monoamine levels, increased hippocampal neurogenesis, release of endorphins directly affecting mood, decrease in cortisol levels, distraction from depressive symptoms and stimuli, and increase in self-efficacy. Though these theories

have been put forth to explain the beneficial effects of physical activity on depression in the general population, it is likely that the mechanisms are similar for prenatal depression.

Few studies have prospectively examined the effect of physical activity on depression or depressive symptoms during pregnancy. The majority of studies conducted have been cross-sectional which raises concerns about temporality. The few prospective studies conducted suggest an inverse effect, though the studies were subject to a number of limitations. In addition, the studies were conducted predominantly among White Non-Hispanic women with little research conducted among Hispanic women.

Our study prospectively and cross-sectionally examined the effect of physical activity on prenatal depression at multiple timepoints during pregnancy using validated measures in a population of pregnant Hispanic women that were predominantly Puerto Rican. We used a depression assessment measure that took into account symptoms of pregnancy. We also assessed various domains and levels of physical activity to better understand the relationship between physical activity and depression in this high-risk population.

Specific Aim and Hypothesis

Specific Aim: To examine the association between physical activity and depression during pregnancy among Hispanic women

Hypothesis 1: Physical activity will be inversely associated with depression during pregnancy among Hispanic women.

Methods

Study Design and Population

Our study examined the association between physical activity and depression during pregnancy using data from Proyecto Buena Salud (PBS), a prospective cohort study conducted from 2006-2011. The study was based at Baystate Medical Center, a large tertiary care center in Western Massachusetts, which has approximately 4,500 deliveries per year and serves an ethnically and socioeconomically diverse population. PBS was approved by the University of Massachusetts, Amherst and Baystate Medical Center Institutional Review Boards. Details about the study design have been published previously.[5]

Briefly, women were recruited in early pregnancy at prenatal care visits (up to 20 weeks gestation). All participants read and signed a written informed consent approved by the Institutional Review Boards at the University of Massachusetts-Amherst and Baystate Medical Center. Interviews were conducted by trained, bilingual interviewers in English or Spanish depending on patient preference. Eligibility for PBS was restricted to women of Puerto Rican or Dominican Republic ancestry, specifically, women that were either: 1) born in Puerto Rico or the Dominican Republic themselves; or 2) had at least one parent or both grandparents born at either of these two locations. As PBS was initially conducted to assess the relationship between pregnancy factors and gestational diabetes, other exclusion criteria included: multiple gestation; history of diabetes, hypertension, heart disease or chronic renal disease; less than 16 or greater than 40 years of age; and current use of medications thought to adversely affect glucose tolerance. Women were interviewed at three timepoints during pregnancy: (1) early pregnancy (≤18

weeks gestation), (2) mid-pregnancy (19-26 weeks gestation), and (3) late pregnancy (>26 weeks gestation). For some women, interviews were not able to be conducted for all of the pregnancy periods.

At initial interview, participants completed depressive symptom and physical activity questionnaires and provided information on sociodemographic, acculturation, and other behavioral and psychological factors. Information was updated at the two subsequent interviews. Medical records were abstracted after delivery for information on medical history and pregnancy information. Among the PBS participants, 1,262 met the study inclusion criteria and had information on physical activity and depressive symptoms. Women were included if they had information on physical activity and depressive symptoms from at least one pregnancy period. Eight hundred and forty-five participants had information on physical activity and depression in early pregnancy, 781 in mid-pregnancy, and 764 in late pregnancy.

Assessment of Physical Activity

Physical activity was assessed at each of the three interviews using a modified version of the Pregnancy Physical Activity Questionnaire (PPAQ).[39] The tool consists of a series of questions asking respondents to indicate intensity, frequency and time spent engaged in 35 activities from four domains: household and caregiving, occupational, exercise and sports, and transportation. For pre-pregnancy activity, participants were asked to report their average physical activity during the year prior to pregnancy; for pregnancy activity, they reported average physical activity over the previous month.

For each pregnancy period (early, mid, late), average overall total physical activity weekly energy expenditure (MET-hrs/wk) was calculated by multiplying the amount of time spent on each activity by its intensity and then summing these values. Activity intensities were determined based on the Compendium of Physical Activities.[40] Those activities identified as having a different intensity during pregnancy were assigned a modified intensity value.[41] In addition, total energy expenditure by domain (household/caregiving, occupational, sports/exercise, transportation) and intensity (light, moderate, vigorous) were calculated. Moderate and vigorous activity were combined into a single category because there were so few women that engaged in vigorous activity. Physical activity levels were categorized into quartiles. As a large percentage of women did not engage in exercise/sports activity during pregnancy, women were categorized into none, physical activity levels "at or below the median," and those "above the median." When examining occupational activity, as unemployed individuals may differ from those that are employed, the analysis was restricted to employed individuals, and physical activity levels were categorized as those "at or below the median" and "above the median."

Physical activity was also categorized as to whether participants met current U.S. HHS physical activity guidelines, which recommend that pregnant women get at least 150 minutes per week of moderate intensity aerobic physical activity.[10] Women were categorized as meeting the guidelines if they participated in an average of 7.5 Met-hrs per week of moderate or vigorous intensity physical activity. Women were also categorized based on whether they met the guidelines when only examining sports/exercise physical

activity. This cut-point was determined by multiplying 2.5 hours (150 minutes) by the lower met limit of moderate intensity activity (3.0 Mets).

The PPAQ has demonstrated good reliability and reasonable validity when compared to Actigraph accelerometer measures.[39] Intra-class correlations (ICCs) for two administrations of the PPAQ one week apart were 0.78, 0.82 and 0.81 for total, moderate and vigorous physical activity, and 0.83, 0.86 and 0.93 for sports/exercise, household/caregiving and occupational activity, respectively. Comparisons between the PPAQ and Actigraph data categorized by cut-points identified in previous studies had Spearman correlations for total, domain specific and intensity level specific physical activity as follows: 0.08 to 0.43 for total activity, -0.08 to 0.22 for light activity, 0.20 to 0.49 for moderate activity, 0.25 to 0.34 for vigorous activity, -0.12 to 0.14 for household activity, -0.10 to 0.42 for occupational activity, and 0.30 to 0.44 for sports/exercise.

Assessment of Depression

The Edinburgh Postnatal Depression Scale (EPDS)[42] was used to assess depressive symptoms at each interview. The questionnaire was administered in English or Spanish depending on participant preference. The EPDS consists of 10 items asking respondents to indicate how frequently they have felt various mood states during the past seven days. Examples of items on the EPDS include, "I have been so unhappy that I have been crying," and "Things have been getting on top of me." Responses are on a 4-point scale ranging from "no, never" to "yes, most of the time" with corresponding scores of 0 (never) to 3 (most of the time). Scores are summed with total scores ranging from 0-30. Scores of 13 or higher are indicative of likely depression (minor or major) and those 15

or higher indicate likely major depression.[43] For each pregnancy period (early, mid, late), women were categorized as to whether or not they had any likely depression (minor or major) or likely major depression. Imputation was used for the EPDS if participants were missing fewer than 10% of items (one EPDS question),[44] which consisted of replacing the missing value with the participant's average score of the nonmissing EPDS items. Depression scores were analyzed categorically (any likely depression, likely major depression) and with depressive symptoms as a continuous variable.

The EPDS has been validated as a depression screening tool in English speaking pregnant women[45] and as a post-natal depression screening tool among European Spanish women.[46] Recommended cut-off scores vary for postnatal and antenatal depression. The recommended cut-off score for antenatal depression in English speaking populations has been identified as ≥15 for major depression (sensitivity=100%; specificity=96-99%) and ≥13 for any depression (minor or major) (sensitivity=57%; specificity=98%) using Research Diagnostic Criteria assessed through Goldberg's Standardized Psychiatric Interview as the gold standard.[43, 47-49] These cut-points were used for this study as the majority of study participants were English speaking and no studies identified to date have validated cut-points for antenatal depression in a Spanish speaking population. In addition, studies validating the EPDS for post-natal depression in Spanish-speaking populations using the recommended cut-points for English-speaking populations have found reasonable sensitivity and specificity for any depression (minor or major) (sensitivity=79%; specificity=96%) and major depression (sensitivity=83%; specificity=97%) when compared to DSM-IV criteria assessed through the Structured Clinical Interview for Axis I DSM Disorders.[46]

Confounders

A number of sociodemographic, acculturation, behavioral, and physical and psychological factors were assessed as covariates. Information on sociodemographic and acculturation covariates was primarily obtained at the initial pregnancy interview. Sociodemographic covariates included maternal age, education level, income and whether the study participant was living with a partner. Level of acculturation covariates included 1) birthplace of participant, parents, and grandparents, and 2) overall degree of acculturation, which was assessed via the Psychological Acculturation Scale (PAS).[50] The PAS is a 10-item scale with responses ranging from 1-5 with lower scores reflective of a Hispanic/Latina orientation and higher scores indicative of an Anglo-American orientation. Average scores less than 3 were categorized as "low acculturation" and those greater than 3 as "high acculturation." Physical, health history and pregnancy factors were obtained by self-report during the initial interview and through medical record abstraction and included: pre-pregnancy weight, height, and morning sickness during pregnancy. BMI was calculated using reported height and weight. Pre-pregnancy and early pregnancy smoking was assessed at initial interview and then updated at subsequent interviews.

Data Analysis

The distributions of early, mid and late pregnancy physical activity and depression measures were evaluated. Physical activity distributions were examined for overall total physical activity, domain-specific levels and intensity-specific levels.

Associations between covariates and physical activity and depression were examined via chi-square tests, t-tests, and ANOVA as appropriate. When expected cell counts for categorical variables were less than five, Fisher's Exact Tests were conducted.

Multivariable logistic regression was used to assess associations between overall total physical activity and depression both cross-sectionally (physical activity and depression from same pregnancy period) and prospectively (physical activity in given pregnancy period with depression in following pregnancy period). These analyses were repeated for each physical activity domain and intensity level and by whether women met the HHS physical activity guideline recommendations.

Age, education and living with a partner/spouse were included as *a priori* confounders in all regression models as they have been identified as risk factors for depression, or in the case of living with a partner/spouse, as a proxy for a strong risk factor (social support).[51, 52] Depression in the prior pregnancy period was included *a priori* in prospective analyses as prior depression has been found to be a strong predictor of prenatal depression.[36, 53] Other potential confounders were included in the model if the odds ratio between the given physical activity variable and depression changed by more than 10% when the confounder was included in the model. In adjusted prospective models, the time interval between interviews was included as a confounder. When examining domains of physical activity, we also adjusted for all other physical activity expenditure, which consisted of the total physical activity energy expenditure minus the expenditure for the given domain of interest. If more than 35 participants were missing values for a given confounder, a missing category was used for that confounder in analyses.

As total physical activity was only calculated when women had data for all of the domains of physical activity, a sensitivity analysis was conducted to determine if the association between total physical activity and the depression measures changed in unadjusted analyses when the missing data was imputed. Multiple imputation was used to create the imputed datasets. Findings were unchanged when analyses were conducted using the imputed datasets.

We also conducted a subanalysis to examine the association between physical activity and incident depression among women that did not have existing depression in the prior pregnancy period. All analyses were conducted using SAS version 9.2 (SAS Institute Inc, Carey, NC).

Results

Study Population Characteristics

Among the 1,414 study participants, the mean age was 22.8 years (SD=5.1)(Table 3.1). Almost half of participants (47%) were born in Puerto Rico or the Dominican Republic and over two thirds of the study population had low levels of acculturation (79%). Women were generally of low socioeconomic status with almost half (48%) reporting that they did not receive a high school diploma or GED. Almost half the women (48%) did not know or did not report annual income with the majority of those reporting having an income of less than $15,000 per year (57%). Half of the participants (51%) reported living with a partner or spouse. Almost half of participants had a pre-pregnancy BMI classified as overweight or obese (46%), and 40% were nulliparous. Just over a

quarter of the participants reported experiencing morning sickness during pregnancy and a third of women reported smoking in the year prior to pregnancy.

Women reported engaging in a median of 56 hours of weekly total physical activity in early pregnancy with median total physical activity energy expenditure in early pregnancy of 137.5 met-hrs/wk (IQR=137.1 met-hrs/wk)(Table 3.2a). The median energy expenditure was lower in mid- and late pregnancy with a median of 122.7 met-hrs/wk (IQR=105.7 met-hrs/wk) in late pregnancy. On average, household physical activity accounted for just over 55% of early pregnancy total energy expenditure among participants, followed by occupational/school activity (20%), transportation (14%) and exercise/sports activities (7%). Almost half of women did not engage in exercise/sports activity in early pregnancy (46%)(Table 3.2c). A third of participants met the HHS pregnancy physical activity guidelines in early pregnancy when using only moderate or vigorous exercise/sports physical activity to categorize compliance, while 80% met the guidelines when using any moderate or vigorous physical activity (Table 3.2b).

The overall mean EPDS score during pregnancy was 8.38 (SD= 5.5). Mean depressive symptom scores were highest in early pregnancy and decreased over the course of pregnancy (Table 3.3a). Over a quarter of women (28.5%) had any likely depression in early pregnancy, with a similar decrease over the course of pregnancy (late pregnancy – 19.5%). Approximately 18% of women were categorized as having likely major depression in early and mid-pregnancy, with the percentage of women likely experiencing this disorder dropping to 13.2% in late pregnancy. When examining patterns of depression during pregnancy across pregnancy periods, among women with early and mid-pregnancy depression data, the majority of women (62.8%) did not

experience any likely depression during either pregnancy period, 13.9% of women experienced likely depression during both pregnancy periods, and 9.3% and 13.9% experienced any likely depression only during either the early or mid-pregnancy periods, respectively (Table 3.3b). We did not examine patterns across all three pregnancy periods due to the limited number of women with data for all periods.

Physical Activity and Covariates

In bivariate analyses examining the associations between physical activity during pregnancy and the potential covariates, income and parity were significantly associated with physical activity across all pregnancy periods (Table 3.4). The lowest activity levels were observed among nulliparous women, and women that did not know or refused to report their income. Younger women had the lowest physical activity levels during all pregnancy periods, though this was only found to be significantly lower in early ($p=0.01$) and late pregnancy ($p<0.01$). Women with a BMI less than 18.5 (underweight) had the lowest levels of physical activity in early pregnancy, whereas those that had a BMI of 18.5 – 25.0 (normal) had the lowest levels of physical activity in mid-pregnancy. Early pregnancy physical activity levels were highest among women who were second generation in mainland U.S. (parent born in Puerto Rico/Dominican Republic) when compared to women that were first or third generation, and among women that lived with a partner or spouse. Women that experienced morning sickness had higher levels of mid-pregnancy physical activity than woman that did not report morning sickness. No other associations were observed between physical activity and covariates.

Depression and Covariates

Income and pre-pregnancy smoking were associated with depressive symptom scores across all pregnancy periods (Table 3.5). Higher levels of depressive symptoms were observed among women that reported an income less than $15,000 when compared to those with greater income, and among pre-pregnancy smokers. Lower levels of early pregnancy depressive symptoms were observed among women that were age 30 or older when compared to younger women, and among those that had an education level greater than a high school degree or GED. Women living with a partner or spouse had lower levels of depressive symptoms in early and mid-pregnancy than those that did not. Finally, early pregnancy depressive symptoms were lower among women that were nulliparous as compared to parous women, and among those that were third generation on the mainland U.S. (grandparent born in Puerto Rico or Dominican Republic) as compared to those who were first or second generation on the mainland. No other associations were observed between depressive symptom scores and covariates.

Physical Activity and Depression

Total Physical Activity

In unadjusted and adjusted multivariable cross-sectional analyses, no associations were found between total physical activity energy expenditure and depressive symptoms, any likely depression, or likely major depression in early, mid- or late pregnancy (Table 3.6). In prospective analysis, total pre-pregnancy physical activity energy expenditure was positively associated with likely depression in early pregnancy in unadjusted and adjusted analyses (Table 3.7). Women in the highest quartile of total physical activity

had 1.81 times the odds (95% CI=1.20, 2.81) of likely depression when compared to women in the lowest quartile in adjusted analysis, which was comparable to the findings of the unadjusted analysis (OR=1.81, 95% CI=1.14, 2.87; p-trend=0.02). Though higher levels of pre-pregnancy total physical activity were also found to increase risk for depressive symptoms and likely major depression, findings were not statistically significant. Higher levels of total mid-pregnancy physical activity were positively associated major depression in adjusted analyses with women in the highest quartile of total physical activity having an OR=3.15 (95% CI=1.06, 9.41) when compared to women in the lowest quartile. The OR increased to 3.89 (95% CI=1.15, 13.19; p-trend=0.03) after adjusting for likely major depression in mid-pregnancy. Early pregnancy total physical activity was not found to be associated with any of the depression outcomes.

Domain of Physical Activity

In cross-sectional analyses, women in the highest quartile of pre-pregnancy household activity had a 55% greater odds of any likely depression in unadjusted analyses (OR=1.55, 95% CI=1.04, 2.31) compared to women in the lowest quartile, though the effect was attenuated and no longer significant in adjusted analyses (Table 3.8); women in the middle quartiles did not have an elevated OR relative to the lowest quartile. Late pregnancy occupational physical activity among workers was inversely associated with likely major depression with those above the median of occupational activity having an OR of 0.41 (95% CI=0.17, 0.96) and an OR of 0.35 (95% CI=0.14, 0.92) compared to workers with occupational physical activity levels below the median in

unadjusted and adjusted analyses, respectively. Late pregnancy household physical activity energy expenditure was positively associated with late pregnancy likely major depression in unadjusted analyses with women in the upper three quartiles having just over two times the odds of likely major depression compared to women in the lowest quartile (Q4 OR=2.04, 95%CI=1.05, 3.95)(Table 3.8). However, this association was attenuated and no longer significant after adjusting for confounders.

In prospective analyses, increasing levels of pre-pregnancy household activity increased risk for any depression in unadjusted analyses (Q4 OR=2.16, 95% CI=1.43, 3.25) and analyses adjusting for potential confounders (Q4 OR=1.89, 95% CI=1.19, 3.00), though the effect was only significant among women in the highest quartile of household physical activity (Table 3.9). However, after adjusting for all other forms of energy expenditure, the estimate of effect was attenuated and no longer significant (OR=1.58, 95% CI=0.96, 2.60). Pre-pregnancy household physical activity was not associated with depressive symptoms (continuous) or likely major depression. Women in the highest quartile of pre-pregnancy transportation physical activity were also at increased odds for depressive symptoms ($beta_{adj}$=2.36, 95% CI=1.33, 3.38) and any likely depression (OR_{adj}= 1.67, 95% CI=1.06, 2.62) in unadjusted and adjusted analyses. These women also had increased odds of likely major depression in adjusted analyses (OR=1.73, 95% CI=1.08, 2.79), though the association was attenuated and no longer significant after additionally adjusting for all other forms of physical activity energy expenditure (OR=1.42, 95% CI=0.83, 2.41). No other associations were observed in prospective analyses examining domain-specific physical activity levels (household/caregiving, occupational, sports/exercise, transportation) and depression.

Light and Moderate/Vigorous Physical Activity

In cross-sectional analyses, no associations were observed between light or moderate/vigorous physical activity and depressive symptoms, likely depression, or likely major depression (Table 3.10). In prospective analyses, pre-pregnancy moderate/vigorous physical activity was positively associated with any likely depression in unadjusted and adjusted analyses with those in the highest quartile having an odds of any likely depression 69% greater than those in the lowest quartile in adjusted analysis (OR=1.63, 95% CI=1.04, 2.54)(Table 3.11). The association was attenuated and no longer significant after additional adjustment for all other physical activity (OR Q4=1.37, 95% CI=0.84, 2.25). No other associations were found between light or moderate/vigorous physical activity levels and any of the depression measures in prospective analyses.

Meeting Pregnancy Physical Activity Guidelines

In cross-sectional analysis, women that met HHS pregnancy physical activity guidelines in late pregnancy using exercise activity alone were at increased risk for major depression in late pregnancy in adjusted analysis (OR=1.62, 95% CI=1.03, 2.55)(Table 3.12). No other associations were found in cross-sectional analysis between meeting the guidelines (using all activity or exercise alone to categorize) and any of the depression measures. In prospective analysis, no associations were observed between meeting HHS physical activity guidelines and depressive symptoms, any likely depression, or likely major depression.

Physical Activity and Subsequent Incident Depression among Women without existing Depression

In prospective unadjusted analyses, there were no associations between any of the physical activity measures in early pregnancy and depression in mid pregnancy (Table 3.13). However, after adjusting for confounders and all other physical activity energy expenditure in domain-specific analyses, women that engaged in early pregnancy exercise physical activity had fewer mid-pregnancy depressive symptoms compared to those that did not engage in exercise physical activity (≤median: beta=-1.21, 95% CI=-2.52, 0.11; >median: beta=-1.51, 95% CI=-2.85, -0.17). Similarly, women that engaged in early pregnancy exercise physical activity were less likely to have likely major depression in mid-pregnancy compared to those that did not engage in physical activity (≤median: OR=0.39, 95% CI=0.14,1.10; OR=0.36, 95% CI=0.13, 0.96). Though the OR was also indicative of a protective effect for any likely depression, the findings were not significant. There were no associations between any mid-pregnancy physical activity measures and any late pregnancy depression measures. Power was limited to detect associations in these analyses due to small sample size.

Discussion

In this prospective cohort of Puerto Rican Hispanic women, we found few associations between physical activity and depression during pregnancy in adjusted analyses. We did not find that total physical activity was inversely associated with depression in prospective analyses as hypothesized. Rather, we found that mid-pregnancy total physical activity was positively associated with late pregnancy likely

major depression after adjusting for important risk factors for depression. High levels of pre-pregnancy total physical activity were also positively associated with early pregnancy likely depression in adjusted analyses. In adjusted analyses examining domain specific physical activity, high levels of pre-pregnancy transportation physical activity were positively associated with early pregnancy depressive symptoms and any likely depression. We did not observe any associations in prospective analyses for any other forms of domain-specific physical activity (household, occupational, exercise) or for intensity level specific physical activity (light, moderate/vigorous) in adjusted analyses. However, when we evaluated associations between physical activity and subsequent incident depression in later pregnancy time periods among women without existing depression, we found that early pregnancy exercise physical activity was inversely associated with depressive symptoms and any likely depression in adjusted analyses. We did not observe any associations between meeting HHS pregnancy physical activity guidelines and depression in prospective analyses.

In terms of the cross-sectional analyses, late pregnancy occupational physical activity was inversely associated with likely major depression among workers. In addition, women that met the HHS physical activity guidelines with exercise activity in late pregnancy had greater odds of late pregnancy likely major depression in adjusted analyses. No other associations were observed between any physical activity measures and any depression outcome measures in adjusted cross-sectional analyses.

Few studies have examined the association between physical activity and depression during pregnancy; the majority were cross-sectional studies focused on leisure time or exercise activity. Among those with a prospective design, two were

observational with Demissie et al.[36] finding a protective effect of moderate/vigorous activity at 17-22 weeks gestation on elevated depressive symptoms at 24-29 weeks gestation, and the other finding no association between exercise during pregnancy and depressive symptoms in the following trimester.[21] The other two prospective studies were a quasi-experimental study and randomized-control-trial, with both finding that the group that received the exercise intervention experienced decreased depressive symptoms.[22, 23] The remaining studies have been cross-sectional with all but one focused on exercise or leisure time activity and the majority reporting an inverse association;[15, 18, 19] two found no association.[16, 20]

Women in our study with greater levels of total mid-pregnancy physical activity were at increased risk for late pregnancy likely major depression in adjusted prospective analyses. Unlike the majority of the other studies conducted during pregnancy, we examined total physical activity that included a variety of domains such that included non-optional childcare, household, and transportation activities. In contrast, the majority of studies conducted have focused on exercise or leisure time activity, which likely explains differences between our study findings and those of the majority of prospective studies.[20, 22] Though Demissie et al. found a protective effect of moderate/vigorous activity in their study, their study population was a highly educated, higher income, predominantly White population that engaged in greater levels of leisure time or recreational physical activity than women in our study.[36] The women in our study were predominantly low SES with the majority of their total physical activity from household physical activity and exercise activity making up only 6-8% of physical energy expenditure across pregnancy, and household/caregiving physical activity accounting for

the majority. We found that women with elevated levels of mid-pregnancy household physical activity had a greater odds of likely major depression which likely contributed to the elevated risk also observed for total physical activity.

Greater levels of household activity may be stressful for women, which could increase risk for depression. It is important to understand whether specific domains of activity, such as household activity, may increase risk of depression as current HHS recommendations call for 150 minutes of moderate physical activity and some examples used are household activities (e.g. mowing the lawn).[25] Molarius et al. found that the more burdensome that study participants perceived domestic activities, the greater the risk for depressive symptoms.[54] Demissie et al. found that women with moderate levels of indoor and high levels of outdoor moderate/vigorous household activity had elevated odds of depressive symptoms compared to women that did not have moderate/vigorous activity in these domains in the only other study to examine domain of physical activity and depression during pregnancy.[36] Similarly, our findings that high levels of pre-pregnancy transportation physical activity increased risk for early pregnancy likely depression could also be a result of increased stress of having to walk for transportation purposes. However, we were not able to adjust for depression in the prior period in our analyses examining pre-pregnancy physical activity and early pregnancy depression. As adjustment for depression modified the association between physical activity measures and depression in some of our analyses, this is a potential limitation of this finding.

Several neurobiological and psychological pathways have been suggested as potential mechanisms to explain how physical activity may prevent or remediate depression/depressive symptoms. Theorized neurobiogic pathways have primarily

focused on physical activity leading to an increase in monoamines, hippocampal neurogenesis, or B-endorphins.[24, 30, 55] Monoamines and hippocampal neurogenesis are believed to be potential pathways as some studies suggest that physical activity increases monoamine levels and hippocampal neurogenesis, both of which are factors associated with the treatment or manifestation of depression. B-endorphins have been associated with feelings of euphoria after extended periods of exercise leading some to believe that this release of endorphins may relieve depressive symptoms. Psychological theories have focused on physical activity or exercise increasing self-efficacy and counteracting negative thinking patterns associated with depression, and exercise as a distraction from negative thoughts associated with depression. Findings from studies that suggest that potential stress inducing domains of physical activity, such as household physical activity, increase risk for depression[36, 37] suggest that the psychological mechanisms likely play a role in reducing depression or depressive symptoms.

We found that early pregnancy exercise physical activity decreased risk for incident mid-pregnancy depressive symptoms and likely major depression among the subset of women that did not have any likely depression in early pregnancy. We found a similar protective effect for any likely depression, though the findings were not significant, which may have been due to small sample size and limited power. This protective effect was not observed in analyses that included the full study sample (i.e. both women with and without existing depression). These findings suggest the possibility that exercise may be more effective at preventing depression during pregnancy among women that are not depressed. The effect of physical activity on depression may vary by level of depression with some arguing that it is effective in treatment for mild-to-

moderate depression.[30] Conversely, studies suggest that it may not be as effective in treatment of major depression. A systematic review by Danielsson et al. found that studies examining physical activity as a treatment for major depression did not support the efficacy of physical activity as a stand-alone treatment, but suggest that it may be effective as an adjunct to treatment.[56] Observational studies that have prospectively examined the association between physical activity and depression or depressive symptoms have generally done so among general populations that included both depressed and non-depressed patients. Some have adjusted for prior depression, while others did not. More research is needed to better understand whether the effects of physical activity differ in the prevention and treatment of depression and whether adjustment for prior depression is appropriate.

This study is one of few studies to prospectively examine the effects of physical activity on depression among pregnant women and the only study to examine this effect in a population of Hispanic women. We used a physical activity measure (PPAQ) designed for use and validated among pregnant women. Similarly, depression was assessed using a measure that takes into account somatic symptoms of pregnancy (EPDS). It is the only study of physical activity and depression during pregnancy to examine the associations among women that did not have depression in the prior pregnancy period and one of few studies in pregnant or non-pregnant populations to examine the effects of domain of physical activity on depression.

Our study has several potential limitations. It is likely that nondifferential misclassification of physical activity occurred as self-report was used to collect average frequency and duration of activities over the course of the previous month or year and it

is likely that the reported amount did not accurately reflect the actual amount. In addition, it is possible that women overreported their physical activity level as a study by Nicaise et al. found overreporting of self-reported physical activity levels in a population of low-income Latina women.[57] Thus, our analyses of the physical activity measure that categorized women as to whether they met HHS guidelines would likely be biased to the null as it used absolute levels of physical activity to categorize women. Analyses that used relative measures of physical activity (e.g. quartiles) would also potentially be biased towards the null.

It is possible that misclassification of depression occurred as the EPDS has not been validated in a Spanish speaking population in the U.S. for antepartum depression screening.[47] Though the EPDS has been validated for post-partum depression in a Spanish speaking population from Spain using the English speaking cut-offs and found good sensitivity and specificity (at least minor: sensitivity=83%, specificity=97%; major: sensitivity=79%; specificity=96%),[46] differences in accuracy by descent and country of residence may occur as a result of slight differences in language and/or interpretation of terms and also cultural differences in the manifestation of depression.[58, 59] However, it is unlikely that this misclassification occurred to a large degree as the sensitivity and specificity of the Spanish version of the EPDS using the validated English language cut-points were good when assessing post-partum depression (at least minor: sensitivity=83%, specificity=97%; major: sensitivity=79%; specificity=96%).[46] As the English version of the EPDS has been demonstrated to have good sensitivity and specificity for detecting antenatal major depression (sensitivity=100%; specificity=96%), and reasonable sensitivity and specificity for detecting any likely antenatal depression

(sensitivity=57%; specificity=98%), we anticipate relatively comparable sensitivity and specificity for the Spanish speaking version in this pouplation.[48]

In prospective analyses, it is possible that selection bias occurred, as we did not have complete physical activity and depression data for women across pregnancy. Participants experiencing high levels of depression or stress may have been more likely to have missing data or drop out of the study because of their high depression or stress levels. Women with depression are also likely to be less active as symptoms of depression include anhedonia and lack of energy. If women missing data were more likely to be both depressed and inactive, then this would bias a protective effect towards the null. If the association were null, then this could bias the results away from the null so that there would appear to be increased risk. Examination of depression levels in the prior pregnancy period among participants with and without depression data suggests that is possible that this occurred in later pregnancy. Among women missing late pregnancy depression data, the prevalence of mid-pregnancy major depression was slightly higher (20.8%) when compared to women that did have late pregnancy data (17.2%). In addition, a larger proportion of women missing late pregnancy depression data engaged in no mid-pregnancy exercise physical activity (40.2%) as compared to women with late pregnancy data (36.0%). Though exercise activity was not significantly associated with depression at any timepoint, estimates of effect were positive when examining mid-pregnancy and late pregnancy depression, which could have occurred as a result of this bias.

Women in this study are asked to self-report information about physical activity and depression. It is possible that women that are experiencing depression may be more

likely to underestimate their physical activity levels as depression may lead to distorted/negative perception. If this were to happen, then the results would be biased such that there would appear to be a more protective effect of physical activity on depression in cross-sectional analysis. For the prospective analysis, it is unlikely that information bias occurred as it would primarily occur due to depression being measured more carefully among those that are physically active. As structured, standardized interviews were used to assess depression, this is unlikely to have occurred.

Our analyses included cross-sectional analyses. Inherent to cross-sectional analyses are concerns of temporality. Thus, our findings from cross-sectional analyses that meeting late pregnancy HHS guidelines (using exercise activity to define compliance) was positively associated with likely major depression and that late pregnancy occupational activity was inversely associated with likely major depression are subject to uncertainty because it is unclear whether the physical activity occurred before the depression or vise versa.

A number of confounders were assessed when examining the relationship between physical activity and prenatal depression. We adjusted for several known risk factors for depression, including depression in the prior pregnancy period. However, we could not adjust for income as a number of women refused to provide income information or were not sure. Income is positively associated with physical activity and also inversely associated with depression with low-income women at greater risk for depression. We did adjust for education, which is correlated with income, so there would be partial adjustment. In cases where there were a protective effect, then the protective

effect would be overestimated. If there were a null effect, then the estimate of effect would be biased away from the null.

The results of this study will most likely be able to be generalized to pregnant women. Hormonal changes during pregnancy may influence the physiologic mechanisms by which physical activity acts on depression potentially limiting generalizability to non-pregnant women. As it is possible that effects of physical activity may vary among nondepressed and depressed women and by severity of depression, then the results may only apply to the subset of the population for which the specific results are relevant. Our findings that total physical activity increased risk for likely major depression would only be applicable to populations that had similarly high proportions of household activity and other forms of activity that may be potentially stressful.

Conclusion

Few studies have prospectively examined the association between physical activity and depression during pregnancy, particularly among high-risk populations that experience high rates of depression. Physical activity is a possible mechanism to both prevent and treat depression in this high-risk population. It is important to find depression treatment alternatives to medication as many women and providers are hesitant to use antidepressants during pregnancy. We did not find that total physical activity, domain specific physical activity or moderate-vigorous physical activity protected against or remediated depression in a high-risk population of Hispanic women with a high prevalence of depression that engaged in very little exercise and whose primary source of physical activity was household/caregiving activity. Our findings do

suggest the possibility that exercise physical activity may be protective among women that do not have depression, but larger studies are needed to more carefully examine whether exercise can prevent the onset of depression and its role in treating depression among pregnant women.

Table 3.1 Participant characteristics: Proyecto Buena Salud, 2006-2011 (n=1414)

Categorical Measures	n	%
Maternal Age		
16-19	445	31.5
20-24	550	38.9
25-29	253	17.9
≥30	166	11.7
missing	0	
Pre-Pregnancy BMI		
less than 18.5	86	6.3
18.5-<25.0	652	47.5
25.0-<30.0	321	23.4
30 or greater	313	22.8
missing	42	
Education		
Less than high school	641	47.8
High school graduate or GED	428	31.9
Post high school	271	20.2
missing	74	
Income		
less than $15,000	401	30.2
$15,000-$30,000	203	15.3
$30,000 or greater	94	7.1
Don't Know/Refused	630	47.4
missing	86	
Parity		
0 live births	573	41.6
1 live birth	423	30.7
2 or more live births	380	27.6
missing	38	
Acculturation		
Low	1007	79.0
High	268	21.0
missing	139	
Generation in U.S.		
Born in PR/DR	640	46.7
Parent born in PR/DR	650	47.4
Grandparent born in PR/DR	81	5.9
missing	43	
Live with Partner/Spouse		
no	649	48.9
yes	677	51.1
missing	88	
Morning Sickness during Pregnancy		
no	1037	73.3
yes	377	26.7
missing	0	
Pre-Pregnancy Smoking		
no	897	66.8
yes	445	33.2
missing	72	
Early Pregnancy Smoking		
no	839	85.9
yes	138	14.2
missing	437	

Table 3.2a Distribution of physical activity in the study population:Proyecto Buena Salud, 2006-2011 (n=1414)

	Pre-Pregnancy met-hrs/wk					Early Pregnancy met-hrs/wk					Mid-Pregnancy met-hrs/wk					Late Pregnancy met-hrs/wk				
Phsical Activity (met-hrs/wk)	**n**	**mean**	**sd**	**median**	**IQR**	**n**	**mean**	**sd**	**median**	**IQR**	**n**	**mean**	**sd**	**median**	**IQR**	**n**	**mean**	**sd**	**median**	**IQR**
Total physical activity	1197	269.8	197.8	219.2	180.9	955	168.9	136.5	137.5	137.1	813	159.8	122.6	127.5	122.5	760	142.5	94.3	122.7	105.7
Domain of Activity																				
Household/caregiving	1265	127.6	110.9	96.7	115.0	979	92.0	92.2	67.4	89.0	843	90.5	83.0	66.9	87.4	782	82.4	68.8	63.3	75.3
Occupation	1252	64.6	73.4	51.8	89.6	1002	36.4	53.1	8.9	63.0	843	30.2	47.0	0.0	50.1	785	23.6	38.2	0.0	44.8
Sports/exercise	1271	39.6	68.2	14.0	42.6	1007	13.4	32.0	1.6	13.5	849	12.0	28.4	3.1	12.9	794	11.3	19.8	3.1	13.7
Transportation	1290	27.6	35.8	16.6	26.3	1009	20.0	23.0	11.6	21.0	856	20.2	27.6	12.0	16.7	797	18.4	23.7	11.4	16.6
Intensity of Activity																				
Sedentary	1301	20.8	16.4	16.4	20.6	1011	21.4	17.6	16.4	20.7	866	20.4	16.2	15.9	20.7	790	19.6	14.4	15.9	19.8
Light	1222	132.1	78.1	116.1	88.6	969	98.0	66.5	85.4	76.7	824	97.4	61.1	84.3	75.4	771	91.3	51.8	84.0	69.4
Moderate/vigorous	1231	137.0	144.9	97.5	130.4	979	70.5	89.1	39.8	81.5	831	61.9	79.8	35.0	66.5	780	50.9	61.5	28.8	55.7

Table 3.2b Distribution of physical activity in the study population:Proyecto Buena Salud, 2006-2011 (n=1414)

	Early Pregnancy		Mid-Pregnancy		Late Pregnancy	
	n	%	n	%	n	%
Met ACOG Guidelines (all moderate or vigorous activity)						
no	202	20.0	159	18.7	156	19.6
yes	808	80.0	691	81.3	641	80.4
Met ACOG Guidelines (exercise moderate or vigorous activity only)						
no	675	67.0	544	64.1	490	61.7
yes	332	33.0	305	35.9	304	38.3

Table 3.2c Distribution of physical activity in the study population:Proyecto Buena Salud, 2006-2011

	Domain												Intensity Level											
	Total Physical Activity				Household/caregiving				Transportation				Sedentary				Light				Moderate/Vigorous			
	n	%	mean*	SD	n	%	mean*	SD	n	%	mean*	SD	n	%	mean*	SD	n	%	mean*	SD	n	%	mean*	SD
Quartiles																								
Pre-Pregnancy																								
Quartile 1	288	24.1	100.6	30.6	310	24.5	33.0	12.9	326	25.3	4.1	2.0	329	25.3	4.7	2.5	302	24.7	53.7	17.7	302	24.5	23.0	12.4
Quartile 2	305	25.5	179.0	21.5	322	25.5	72.9	12.3	322	25.0	11.6	2.4	330	25.4	12.6	2.5	300	24.6	96.6	10.9	307	24.9	67.2	15.3
Quartile 3	302	25.2	265.6	32.2	317	25.1	127.7	20.3	328	25.4	24.3	4.9	322	24.8	23.1	3.6	312	25.5	138.0	14.4	313	25.4	131.0	23.3
Quartile 4	302	25.2	527.0	225.5	316	25.0	276.0	121.3	314	24.3	71.8	49.3	320	24.6	43.5	14.3	308	25.2	237.5	71.8	309	25.1	324.1	173.8
Early Pregnancy																								
Quartile 1	239	25.0	49.9	21.1	244	24.9	16.7	8.3	294	29.1	3.0	1.8	254	25.1	4.3	2.6	243	25.1	32.0	13.4	245	25.0	4.8	4.4
Quartile 2	238	24.9	107.4	16.5	245	25.0	49.6	10.5	216	21.4	8.9	1.9	253	25.0	12.2	2.4	241	24.9	68.0	9.2	246	25.1	25.8	7.4
Quartile 3	240	25.1	174.1	22.7	247	25.2	90.8	15.2	248	24.6	19.0	4.1	276	27.3	23.6	4.1	244	25.2	105.1	12.1	245	25.0	65.4	16.6
Quartile 4	238	24.9	344.7	156.9	243	24.8	211.6	109.7	251	24.9	50.3	27.3	228	22.6	47.8	14.7	241	24.9	187.3	63.6	243	24.8	187.0	108.0
Mid Pregnancy																								
Quartile 1	202	24.9	50.8	20.2	211	25.0	18.9	8.3	213	24.9	3.3	1.7	215	24.8	4.6	2.2	206	25.0	33.8	13.2	206	24.8	5.4	4.3
Quartile 2	202	24.9	103.8	12.9	208	24.7	47.9	9.4	214	25.0	9.0	1.7	224	25.9	12.3	12.3	205	24.9	69.2	8.4	207	24.9	22.4	5.8
Quartile 3	207	25.5	162.7	22.3	211	25.0	90.2	14.8	217	25.4	17.5	3.4	226	26.1	22.7	22.7	207	25.1	104.9	12.5	210	25.3	54.7	12.9
Quartile 4	202	24.9	321.7	135.0	213	25.3	203.3	85.6	212	24.8	51.4	40.9	201	23.2	43.7	43.7	206	25.0	181.7	50.1	208	25.0	164.2	100.0
Late Pregnancy																								
Quartile 1	190	25.0	52.4	19.4	196	25.1	20.4	9.0	203	25.5	3.4	1.6	209	26.5	5.3	2.7	193	25.0	34.4	12.7	200	25.6	4.9	4.0
Quartile 2	190	25.0	100.0	12.7	196	25.1	49.3	8.5	214	26.9	9.0	1.8	204	25.8	13.2	2.1	192	24.9	68.0	8.9	190	24.4	20.0	4.7
Quartile 3	191	25.1	148.2	18.0	196	25.1	84.2	13.0	284	23.1	16.7	3.3	198	25.1	22.3	3.6	193	25.0	101.4	10.0	196	25.1	45.0	10.6
Quartile 4	189	24.9	269.9	92.9	194	24.8	176.7	69.9	296	24.6	45.7	34.5	179	22.7	40.5	12.7	193	25.0	161.5	39.5	194	24.9	134.6	70.0

Table 3.2c Distribution of physical activity in the study population:Proyecto Buena Salud, 2006-2011 (continued)

	Occupational**				Sports/exercise			
	n	**%**	**mean***	**SD**	**n**	**%**	**mean***	**SD**
Other Categorizations								
Pre-Pregnancy								
None	n/a	n/a	n/a	n/a	267	21.0	0.0	n/a
Low (at or below median)	459	49.6	42.4	17.5	498	39.2	10.3	6.3
High (above median)	467	50.4	131.6	79.2	506	39.8	89.2	86.8
Early Pregnancy								
None	n/a	n/a	n/a	n/a	464	46.1	0.0	n/a
Low (at or below median)	262	50.2	35.0	16.7	256	25.4	4.6	2.7
High (above median)	260	49.8	105.1	58.5	287	28.5	42.8	48.7
Mid Pregnancy								
None	n/a	n/a	n/a	n/a	324	38.2	0.0	n/a
Low (at or below median)	196	50.0	33.9	13.9	262	30.9	4.5	2.6
High (above median)	196	50.0	96.0	53.7	263	31.0	34.1	43.3
Late Pregnancy								
None	n/a	n/a	n/a	n/a	299	37.7	0.0	n/a
Low (at or below median)	162	49.4	28.6	14.3	235	29.6	4.6	2.8
High (above median)	166	50.6	83.9	38.8	260	32.8	30.4	25.2

*met-hrs/wk

**Among employed/students

Table 3.3a Distribution of probable depression in the study population:Proyecto Buena Salud, 2006-2011

Depressive Symptoms - Continuous	Mean	SD
Overall Pregnancy (n=1414)	8.38	5.49
Early Pregnancy (n=969)	9.12	5.88
Mid-Pregnancy (n=819)	8.39	6.11
Late Pregnancy (n=794)	7.41	5.80

Depression	n	%
Early Pregnancy		
Any probable depression*		
No	693	71.5
Yes	276	28.5
Probable major depression**		
No	796	82.2
Yes	173	17.9
Mid Pregnancy		
Any probable depression*		
No	613	74.9
Yes	206	25.2
Probable major depression**		
No	663	81.0
Yes	156	19.1
Late Pregnancy		
Any probable depression*		
No	639	80.5
Yes	155	19.5
Probable major depression**		
No	689	86.8
Yes	105	13.2

* EPDS score ≥13
**EPDS score ≥15

Table 3.3b Distribution of probable depression in the study population across pregnancy periods: Proyecto Buena Salud, 2006-2011

	n	%
Early and Mid Pregnancy (n=503)		
At least probable minor depression*		
neither pregnancy period	316	62.8
early pregnancy only	70	13.9
mid-pregnancy only	47	9.3
early and mid-pregnancy	70	13.9
Probable major depression**		
neither pregnancy period	367	73.0
early pregnancy only	47	9.3
mid-pregnancy only	47	9.3
early and mid-pregnancy	42	8.4
Mid and Late Pregnancy (n=396)		
At least probable minor depression*		
neither pregnancy period	266	67.2
mid-pregnancy only	56	14.1
late pregnancy only	33	8.3
mid and late pregnancy	41	10.4
Probable major depression**		
neither pregnancy period	304	76.8
mid-pregnancy only	42	10.6
late pregnancy only	24	6.1
mid and late pregnancy	26	6.6
Early and Late Pregnancy (n=503)		
At least probable minor depression*		
neither pregnancy period	316	62.8
early pregnancy only	79	15.7
late pregnancy only	40	8.0
early and late pregnancy	68	13.5
Probable major depression**		
neither pregnancy period	384	76.3
early pregnancy only	48	9.5
late pregnancy only	33	6.6
early and late pregnancy	38	7.6

*EPDS score ≥13

**EPDS score ≥15

Table 3.4 Distribution of covariates by total physical activity energy expenditure in the study population: Proyecto Buena Salud, 2006-2011

	Total Non-Sedentary Physical Activity Met Scores (met-hrs/wk)								
	Early Pregnancy (n=955)			Mid-Pregnancy (n=813)			Late Pregnancy (n=760)		
	mean	SD	p-value	mean	SD	p-value	mean	SD	p-value
Maternal Age									
16-19	151.8	137.3	0.01	146.8	119.1	0.10	125.5	86.1	<0.01
20-24	173.8	130.6		168.2	133.5		144.1	93.4	
25-29	193.7	149.4		170.1	112.6		163.3	96.9	
>=30	165.5	126.2		149.0	103.5		151.1	108.0	
Pre-pregnancy BMI, 2009 IOM categories									
less than 18.5	136.6	86.4	0.03	179.1	170.8	0.04	118.9	69.0	0.12
18.5-25.0	158.6	125.5		149.9	116.5		141.4	96.9	
25.0-30.0	179.2	150.1		154.4	104.3		140.7	84.4	
30 or greater	184.1	153.3		178.1	133.4		154.2	102.0	
Education									
Less than high school	160.6	147.1	0.11	156.1	129.9	0.36	138.6	89.5	0.43
High school graduate or GED	181.8	138.3		169.3	125.1		148.8	93.9	
Post high school	166.1	101.7		154.7	109.1		145.0	109.2	
Income									
less than $15,000	162.7	130.3	0.03	165.8	120.4	0.04	143.9	100.2	0.04
$15,000-$30,000	191.9	140.6		184.0	114.9		164.6	93.4	
$30,000 or greater	194.4	143.1		171.0	134.4		143.3	92.5	
Don't Know/Refused	161.0	137.7		148.2	128.5		134.6	90.0	
Parity									
0 live births	141.1	128.7	<0.01	133.8	114.8	<0.01	122.0	82.9	<0.01
1 live birth	187.1	127.9		174.6	121.0		159.7	97.8	
2 or more live births	191.1	155.0		182.6	129.8		153.3	101.2	
Acculturation									
Low	166.8	138.8	0.22	161.7	125.4	0.84	142.3	98.0	0.93
High	180.6	134.6		159.3	134.6		143.0	129.6	
Generation in U.S.									
Born in PR/DR	158.2	123.0	0.04	152.5	108.5	0.14	141.7	97.9	0.63
Parent born in PR/DR	181.2	153.4		164.7	129.8		140.0	87.5	
Grandparent born in PR/DR	159.3	92.0		184.3	168.9		155.1	106.7	
Live with partner/spouse									
no	159.8	142.7	0.05	158.1	133.4	0.55	137.7	92.0	0.14
yes	177.4	130.7		163.5	116.1		148.1	96.3	
Morningsickness during Pregnancy									
no	165.3	139.6	0.20	154.5	117.0	0.04	n/a	n/a	
yes	178.0	128.1		174.1	135.9				
Pre-Pregnancy Smoking									
no	164.3	126.2	0.18	159.9	122.6	1.00	141.8	95.6	0.48
yes	176.7	154.9		159.9	127.9		147.1	94.7	

Table 3.5 Distribution of covariates by mean depressive symptom scores in the study population: Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (EPDS score)								
	Early Pregnancy (n=969)			Mid- Pregnancy (n=819)			Late Pregnancy (n=794)		
	mean	SD	p-value	mean	SD	p-value	mean	SD	p-value
Maternal Age									
16-19	8.5	5.4	<0.01	8.5	5.9	0.79	7.2	5.1	0.86
20-24	9.7	6.0		8.2	6.1		7.4	5.9	
25-29	10.0	5.8		8.8	6.6		7.7	6.2	
>=30	7.4	6.3		8.1	6.2		7.5	6.5	
Pre-pregnancy BMI, 2009 IOM categories									
less than 18.5	9.4	5.8	0.45	8.4	6.2	0.24	8.2	6.4	0.11
18.5-25.0	9.3	5.8		8.6	6.1		7.7	5.8	
25.0-30.0	8.6	5.9		7.6	5.6		6.5	5.6	
30 or greater	9.1	5.9		8.7	6.4		7.4	5.8	
Education									
Less than high school	9.8	6.4	<0.01	8.6	6.3	0.37	7.8	6.2	0.14
High school graduate or GED	9.2	5.3		8.1	5.7		7.4	5.4	
Post high school	7.5	5.3		7.8	5.8		6.7	5.3	
Income									
less than $15,000	10.0	6.1	<0.01	9.3	6.5	<0.01	8.4	6.4	<0.01
$15,000-$30,000	8.7	5.7		7.3	5.4		6.6	5.1	
$30,000 or greater	7.6	5.6		7.1	5.7		5.8	5.5	
Don't Know/Refused	8.9	5.8		8.1	5.9		7.3	5.6	
Parity									
0 live births	8.6	5.7	0.05	8.1	5.8	0.44	6.8	5.2	0.07
1 live birth	9.4	5.5		8.4	6.2		7.5	5.5	
2 or more live births	9.6	6.5		8.8	6.4		7.9	6.7	
Acculturation									
Low	9.1	5.8	0.73	8.4	6.1	0.18	7.5	5.8	0.73
High	8.9	5.9		7.7	5.9		7.4	6.0	
Generation in U.S.									
Born in PR/DR	8.7	5.8	0.03	8.2	6.2	0.42	7.3	6.0	0.49
Parent born in PR/DR	9.7	6.0		8.6	6.0		7.5	5.8	
Grandparent born in PR/DR	8.2	4.6		7.4	5.6		6.4	5.2	
Live with partner/spouse									
no	9.6	6.0	0.03	8.8	6.3	0.04	7.6	6.0	0.58
yes	8.7	5.7		7.9	5.7		7.4	5.6	
Morningsickness during Pregnancy									
no	9.0	5.8	0.25	8.3	6.0	0.52	n/a	n/a	n/a
yes	9.5	6.0		8.6	6.4				
Pre-pregnancy smoking									
no	8.5	5.7	<0.01	7.8	5.9	<0.01	6.8	5.3	<0.01
yes	10.3	6.1		9.5	6.3		8.7	6.5	

Table 3.6 Odds ratios of probable depression by total physical activitly level in same pregnancy period:Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (continuous)						At least Probable Minor Depression*						Probable Major Depression**					
			Unadjusted		Adjusted[#]				Unadjusted		Adjusted[#]				Unadjusted		Adjusted[#]	
Total Physical Activity	**mean**	**SD**	**Beta**	**95%CI**	**Beta**	**95%CI**	**n**	**%**	**OR**	**95%CI**	**OR**	**95%CI**	**n**	**%**	**OR**	**95%CI**	**OR**	**95%CI**
Early Pregnancy																		
Continuous			0.00	0.00, 0.01	0.00	0.00, 0.01			1.00	1.00, 1.00	1.00	1.00, 1.00			1.00	1.00, 1.00	1.00	1.00, 1.00
Quartiles																		
1st Quartile	9.04	6.14	ref		1.00	referent	66	29.2	1.00	referent	1.00	referent	46	20.4	1.00	referent	1.00	referent
2nd Quartile	9.00	6.00	-0.04	-1.11, 1.03	0.26	-0.84, 1.36	62	26.6	0.88	0.58, 1.32	0.91	0.59, 1.40	42	18.0	0.86	0.54, 1.37	0.91	0.56, 1.48
3rd Quartile	8.32	5.45	-0.72	-1.79, 0.36	-0.50	-1.61, 0.61	55	24.1	0.77	0.51, 1.17	0.78	0.50, 1.22	28	12.3	0.55	0.33, 0.91	0.58	0.34, 1.00
4th Quartile	10.07	5.83	1.04	-0.04, 2.12	0.90	-0.23, 2.03	80	35.1	1.31	0.88, 1.95	1.19	0.77, 1.83	46	20.2	0.99	0.63, 1.56	0.97	0.59, 1.59
Mid-Pregnancy																		
Continuous			0.00	0.00, 0.00	0.00	0.00, 0.00			1.00	1.00, 1.00	1.00	1.00, 1.00			1.00	1.00, 1.00	1.00	0.99, 1.00
Quartiles																		
1st Quartile	8.68	6.47	ref		1.00	referent	51	26.3	1.00	referent	1.00	referent	41	12.1	1.00	referent	1.00	referent
2nd Quartile	8.21	5.89	-0.47	-1.67, 0.74	-0.73	-1.97, 0.51	42	21.9	0.79	0.49, 1.25	0.70	0.43, 1.14	33	17.2	0.78	0.47, 1.29	0.66	0.39, 1.13
3rd Quartile	7.75	5.98	-0.93	-2.12, 0.26	-1.14	-2.39, 0.11	45	22.4	0.81	0.51, 1.28	0.72	0.44, 1.18	35	17.4	0.79	0.48, 1.30	0.68	0.40, 1.17
4th Quartile	8.88	5.88	0.20	-1.00, 1.40	-0.20	-1.46, 1.07	56	28.6	1.12	0.72, 1.75	0.92	0.56, 1.49	39	19.9	0.93	0.57, 1.52	0.68	0.40, 1.17
Late Pregnancy																		
Continuous			0.00	0.00, 0.01	0.00	0.00, 0.01			1.00	1.00, 1.00	1.00	1.00, 1.00			1.00	1.00, 1.00	1.00	1.00, 1.00
Quartiles																		
1st Quartile	7.04	5.59	ref		1.00	referent	20	20.6	1.00	referent	1.00	referent	12	12.4	1.00	referent	1.00	referent
2nd Quartile	7.69	6.25	0.65	-0.52, 1.82	0.69	-0.53, 1.90	23	23.2	1.12	0.68, 1.85	1.03	0.60, 1.76	16	16.2	1.20	0.68, 2.15	1.20	0.64, 2.27
3rd Quartile	7.31	5.60	0.28	-0.88, 1.44	0.41	-0.82, 1.62	12	12.2	0.80	0.47, 1.35	0.75	0.42, 1.32	9	9.2	0.81	0.44, 1.50	0.77	0.39, 1.52
4th Quartile	7.51	5.71	0.47	-0.70, 1.63	0.42	-0.83, 1.66	16	19.5	1.04	0.63, 1.73	1.01	0.59, 1.75	12	14.6	0.91	0.50, 1.68	0.93	0.48, 1.80

* EPDS score ≥13

**EPDS score ≥15

[#]Adjusted for age, education, live with partner or spouse, generation in the U.S., and parity

Table 3.7 Odds ratios of probable depression by total physical activity level in preceding pregnancy period: Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (continuous)						At least Probable Minor Depression*								Probable Major Depression**							
Total Physical			**Unadjusted**		**Adjusted**[***]				**Unadjusted**		**Adjusted1**[***]		**Adjusted2**[****]				**Unadjusted**		**Adjusted1**[***]		**Adjusted2**[****]	
Activity	**mean**	**SD**	**Beta**	**95%CI**	**Beta**	**95%CI**	**n**	**%**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**	**n**	**%**	**OR**	**95%CI**	**OR**	**95%CI**	**OR**	**95%CI**
Pre-Pregnancy[#]																						
Continuous			0.00	0.00, 0.00	0.00	0.00, 0.01			1.00	1.00, 1.00	1.00	1.00, 1.00	n/a	n/a			1.00	1.00, 1.00	1.00	1.00, 1.00	n/a	n/a
Quartiles																						
1st Quartile	8.03	5.78	ref		ref		46	22.7	1.00	referent	1.00	referent	n/a	n/a	30	14.8	1.00	referent	1.00	referent	n/a	n/a
2nd Quartile	9.09	5.97	1.06	-0.04, 2.16	1.19	0.06, 2.32	65	27.8	1.31	0.85, 2.03	1.36	0.85, 2.17	n/a	n/a	44	18.8	1.34	0.80, 2.22	1.47	0.86, 2.52	n/a	n/a
3rd Quartile	9.06	5.73	1.02	-0.09, 2.13	1.17	0.01, 2.32	63	27.8	1.31	0.85, 2.03	1.34	0.83, 2.16	n/a	n/a	38	16.7	1.16	0.69, 1.95	1.37	0.78, 2.40	n/a	n/a
4th Quartile	10.06	5.94	2.03	0.92, 3.13	2.07	0.94, 3.21	80	34.9	1.83	1.20, 2.81	1.81	1.14, 2.87	n/a	n/a	47	20.5	1.49	0.90, 2.46	1.57	0.91, 2.69	n/a	n/a
Early Pregnancy[##]																						
Continuous			0.00	0.00, 0.01	0.00	0.00, 0.01			1.00	1.00, 1.00	1.00	1.00, 1.00	1.00	1.00, 1.00			1.00	1.00, 1.00	1.00	1.00, 1.00	1.00	1.00, 1.00
Quartiles																						
1st Quartile	8.56	6.35	ref		ref		34	26.6	1.00	referent	1.00	referent	1.00	referent	28	21.8	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	7.38	5.72	-1.18	-2.70, 0.34	-0.67	-2.27, 0.93	17	15.5	0.51	0.26, 0.97	0.56	0.28, 1.11	0.54	0.25, 1.16	11	10	0.40	0.19, 0.84	0.42	0.19,0.94	0.42	0.17, 1.02
3rd Quartile	7.58	5.33	-0.99	-2.44, 0.47	-0.56	-2.11, 0.98	25	18.9	0.65	0.36, 1.16	0.77	0.41, 1.46	0.88	0.44, 1.78	17	12.9	0.53	0.27, 1.02	0.64	0.31,1.30	0.71	0.32, 1.57
4th Quartile	9.33	6.52	0.77	-0.69, 2.23	1.02	-0.56, 2.61	43	33.3	1.38	0.81, 2.36	1.48	0.81, 2.69	1.32	0.67, 2.61	35	27.1	1.33	0.75, 2.35	1.52	0.80, 2.87	1.83	0.90, 3.72
Mid-Pregnancy[###]																						
Continuous			0.00	0.00, 0.01	0.00	0.00, 0.01			1.00	1.00, 1.00	1.00	1.00, 1.00	1.00	1.00, 1.00			1.00	1.00, 1.00	1.00	1.00, 1.01	1.00	1.00, 1.01
Quartiles																						
1st Quartile	6.79	5.39	ref		ref		18	19.4	1.00	referent	1.00	referent	1.00	referent	7	7.1	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	7.68	5.84	0.90	-0.72, 2.52	0.78	-0.93, 2.50	20	21.1	1.19	0.58, 2.41	1.01	0.45, 2.24	0.86	0.36, 2.06	14	14.7	2.25	0.86, 5.84	2.24	0.72, 6.92	2.55	0.75, 8.75
3rd Quartile	6.83	5.74	0.05	-1.55, 1.64	0.06	-1.64, 1.77	19	18.6	1.02	0.50, 2.08	1.05	0.48, 2.31	0.76	0.32, 1.83	16	15.7	2.42	0.95, 6.17	2.81	0.94, 8.39	3.31	0.99, 11.05
4th Quartile	7.53	6.10	0.75	-0.84, 2.34	0.91	-0.80, 2.62	20	19.4	1.07	0.53, 2.17	1.15	0.52, 2.53	0.95	0.40, 2.24	6	15.5	2.39	0.94, 6.09	3.15	1.06, 9.41	3.89	1.15, 13.19

* EPDS score ≥13

**EPDS score ≥15

[***]Adjusted for age, education, live with partner or spouse, parity, generation in U.S., and weeks between interviews (for models examining mid- and late pregnancy depression)

[****]Adjusted for depression in prior pregnancy period

[#] Examining association with early pregnancy depression

[##] Examining association with mid-to-late pregnancy depression

[###]Examining association with late pregnancy depression

Table 3.8 Odds ratios of probable depression by domain of physical activity in same pregnancy period:Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (continuous)						At least Probable Minor Depression*						Probable Major Depression**					
			Unadjusted		Adjusted***				Unadjusted		Adjusted***				Unadjusted		Adjusted***	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Early Pregnancy																		
Household/caregiving																		
1st Quartile	8.61	5.94	ref		ref		60	26.0	1.00	referent	1.00	referent	44	19.1	1.00	referent	1.00	referent
2nd Quartile	8.90	6.00	0.29	-0.77, 1.36	-0.03	-1.16, 1.10	57	24.5	0.92	0.61, 1.40	0.82	0.51, 1.32	40	17.2	0.88	0.55, 1.41	0.74	0.43, 1.27
3rd Quartile	8.89	5.64	0.28	-0.78, 1.34	-0.38	-1.53, 0.77	66	27.9	1.10	0.73, 1.66	0.85	0.53, 1.37	38	16.0	0.81	0.50, 1.31	0.62	0.36, 1.08
4th Quartile	9.93	5.85	1.33	0.26, 2.39	0.48	-0.74, 1.70	82	35.2	1.55	1.04, 2.31	1.23	0.76, 1.99	42	18.0	0.94	0.59, 1.49	0.75	0.43, 1.32
Occupational																		
at or below median	8.27	5.33	ref		ref		57	46.7	1.00	referent	1.00	referent	35	48.0	1.00	referent	1.00	referent
above median	8.63	5.63	0.36	-0.59, 1.32	0.11	-0.87, 1.09	65	53.3	1.24	0.82, 1.87	1.21	0.77, 1.89	38	52.1	1.14	0.70, 1.88	1.09	0.63, 1.89
Sports/Exercise																		
none	9.22	5.88	ref		ref		122	27.8	1.00	referent	1.00	referent	76	17.3	1.00	referent	1.00	referent
at or below median	8.68	5.81	-0.54	-1.46, 0.38	-0.42	-1.35, 0.51	67	27.4	0.98	0.69, 1.39	1.06	0.73, 1.54	41	16.7	0.96	0.63, 1.45	1.02	0.65, 1.59
above median	9.32	5.93	0.10	-0.78, 0.99	-0.27	-1.18, 0.64	85	30.7	1.15	0.83, 1.60	1.03	0.72, 1.48	54	19.5	1.16	0.79, 1.70	1.09	0.71, 1.67
Transportation																		
1st Quartile	8.82	6.16	ref		ref		80	28.6	1.00	referent	1.00	referent	52	18.6	1.00	referent	1.00	referent
2nd Quartile	9.15	5.88	0.33	-0.72, 1.38	0.40	-0.67, 1.47	57	27.8	0.96	0.65, 1.44	1.02	0.67, 1.56	36	17.6	0.93	0.58, 1.49	1.02	0.62, 1.68
3rd Quartile	8.50	5.49	-0.32	-1.32, 0.69	-0.09	-1.13, 0.94	57	24.0	0.79	0.53, 1.17	0.84	0.55, 1.28	34	14.3	0.73	0.46, 1.17	0.80	0.48, 1.33
4th Quartile	9.95	5.75	1.13	0.13, 2.13	1.04	-0.04, 2.11	79	32.9	1.23	0.84, 1.78	1.23	0.81, 1.86	48	20.0	1.10	0.71, 1.70	1.14	0.70, 1.86
Mid-Pregnancy																		
Household/caregiving																		
1st Quartile	8.08	5.83	ref		ref		42	21.2	1.00	referent	1.00	referent	32	16.2	1.00	referent	1.00	referent
2nd Quartile	8.50	6.27	0.43	-0.77, 1.62	0.34	-0.91, 1.59	48	24.2	1.19	0.74, 1.90	1.08	0.64, 1.81	40	20.2	1.31	0.79, 2.19	1.27	0.72, 2.23
3rd Quartile	8.29	6.12	0.22	-0.98, 1.41	-0.21	-1.48, 1.07	52	25.9	1.30	0.82, 2.06	1.10	0.66, 1.85	38	18.9	1.21	0.72, 2.03	1.01	0.57, 1.81
4th Quartile	8.74	6.13	0.66	-0.52, 1.85	0.21	-1.11, 1.53	59	28.9	1.51	0.96, 2.38	1.24	0.73, 2.11	44	21.6	1.43	0.86, 2.36	1.16	0.64, 2.11
Occupational																		
at or below median	7.60	5.78	ref		ref		38	53.5	1.00	referent	1.00	referent	30	57.7	1.00	referent	1.00	referent
above median	7.35	7.35	-0.25	-1.38, 0.88	-0.30	-1.50, 0.89	33	46.5	0.81	0.49, 1.37	0.77	0.44, 1.37	22	42.3	0.68	0.38, 1.22	0.65	0.34, 1.25
Sports/Exercise																		
none	8.36	6.22	ref		ref		78	25.7	1.00	referent	1.00	referent	60	19.7	1.00	referent	1.00	referent
at or below median	8.40	6.29	0.04	-0.97, 1.06	-0.09	-1.11, 0.93	67	26.4	1.04	0.71, 1.52	1.01	0.68, 1.50	49	19.3	0.97	0.64, 1.48	0.90	0.58, 1.40
above median	8.36	5.79	0.01	-1.01, 1.02	0.03	-1.02, 1.08	58	22.8	0.85	0.58, 1.26	0.84	0.55, 1.27	44	17.3	0.85	0.55, 1.30	0.80	0.51, 1.26
Transportation																		
1st Quartile	8.67	6.36	ref		ref		53	26.8	1.00	referent	1.00	referent	41	20.7	1.00	referent	1.00	referent
2nd Quartile	7.91	5.82	-0.76	-1.94, 0.42	-0.65	-1.85, 0.56	45	21.6	0.76	0.48, 1.19	0.79	0.49, 1.27	31	14.9	0.67	0.40, 1.12	0.75	0.44, 1.27
3rd Quartile	7.52	5.89	-1.15	-2.33, 0.03	-1.03	-2.25, 0.19	42	20.4	0.70	0.44, 1.11	0.71	0.44, 1.15	28	13.6	0.60	0.36, 1.02	0.64	0.37, 1.11
4th Quartile	9.38	6.21	0.71	-0.47, 1.89	0.56	-0.72, 1.83	64	31.2	1.24	0.81, 1.91	1.20	0.74, 1.93	54	26.3	1.37	0.86, 2.18	1.40	0.84, 2.35

Table 3.8 Odds ratios of probable depression by domain of physical activity in same pregnancy period:Proyecto Buena Salud, 2006-2011 (continued)

	Depressive Symptoms (continuous)						At least Probable Minor Depression*						Probable Major Depression**					
			Unadjusted		Adjusted***				Unadjusted		Adjusted***				Unadjusted		Adjusted***	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Late Pregnancy																		
Household/caregiving																		
1st Quartile	6.59	5.12	ref		ref		32	16.5	1.00	referent	1.00	referent	15	7.7	1.00	referent	1.00	referent
2nd Quartile	7.35	5.60	0.77	-0.38, 1.91	0.24	-0.99, 1.47	36	18.5	1.15	0.68, 1.94	0.87	0.47, 1.59	29	14.9	2.09	1.08, 4.03	1.62	0.75, 3.51
3rd Quartile	7.73	6.24	1.14	-0.02, 2.29	0.95	-0.28, 2.18	41	21.0	1.35	0.81, 2.25	1.21	0.68, 2.15	30	15.4	2.17	1.13, 4.18	2.00	0.94, 4.23
4th Quartile	7.90	6.05	1.31	0.17, 2.46	1.06	-0.23, 2.34	42	21.9	1.42	0.85, 2.36	1.26	0.69, 2.31	28	14.6	2.04	1.05, 3.95	1.92	0.87, 4.20
Occupational																		
at or below median	7.12	5.56	ref		ref		27	55.1	1.00	referent	1.00	referent	18	69.2	1.00	referent	1.00	referent
above median	6.22	4.92	-0.90	-2.04, 0.24	-1.08	-2.26, 0.09	22	44.9	0.76	0.42, 1.41	0.69	0.35, 1.35	8	30.8	0.41	0.17, 0.96	0.35	0.14, 0.92
Sports/Exercise																		
none	7.09	5.80	ref		ref		61	20.4	1.00	referent	1.00	referent	37	12.4	1.00	referent	1.00	referent
at or below median	7.15	5.54	0.07	-0.92, 1.06	0.21	-0.83, 1.24	40	17.2	0.81	0.52, 1.26	0.82	0.51, 1.32	25	10.7	0.85	0.50, 1.46	1.02	0.57, 1.82
above median	8.00	5.97	0.90	-0.06, 1.86	0.81	-0.19, 1.81	52	20.2	0.99	0.65, 1.50	0.96	0.61, 1.50	41	16.0	1.34	0.83, 2.17	1.48	0.87, 2.53
Transportation																		
1st Quartile	7.69	6.22	ref		ref		49	24.5	1.00	referent	1.00	referent	27	13.5	1.00	referent	1.00	referent
2nd Quartile	6.91	5.98	-0.79	-1.90, 0.33	-0.97	-2.14, 0.19	36	16.8	0.62	0.39, 1.01	0.59	0.35, 0.99	31	14.5	1.09	0.62, 1.89	1.09	0.60, 2.00
3rd Quartile	7.69	5.60	0.00	-1.16, 1.17	-0.06	-1.27, 1.14	32	17.5	0.65	0.40, 1.08	0.66	0.38, 1.12	23	12.6	0.92	0.51, 1.67	0.96	0.50, 1.83
4th Quartile	7.40	5.38	-0.29	1.44, 0.85	-0.43	-1.64, 1.34	38	19.5	0.75	0.46, 1.20	0.75	0.45, 1.27	24	12.3	0.90	0.50, 1.62	1.00	0.53, 1.89

* EPDS score ≥13

**EPDS score ≥15

*** Household PA models adjusted for age of mother, education, live with partner or spouse, parity, BMI, pre-pregnancy smoking, acculturation, all other physical activity expenditure

Occupation PA models adjusted for age of mother, education, live with partner or spouse, all other physical activity expenditure

Occupational (employed only) adjust for age of mother, education, live with partner or spouse, all other physical activity expenditure

Exercise PA models adjusted for age of mother, education, live with partner or spouse, pre-pregnancy smoking, all other physical activity expenditure

Transportation PA models adjusted for age of mother, education, live with partner or spouse, all other physical activity expenditure

Table 3.9 Odds ratios of probable depression by domain-specific physical activity level in preceding pregnancy period:Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (continuous)						At least Probable Minor Depression*								Probable Major Depression**							
			Unadjusted		Adjusted***				Unadjusted		Adjusted1***		Adjusted2****				Unadjusted		Adjusted1***		Adjusted2****	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI
Pre-Pregnancy#																						
Household/ caregiving																						
1st Quartile	8.29	5.78	ref		1.00	referent	49	22.1	1.00	referent	1.00	referent	1.00	referent	38	17.1	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	8.83	5.86	0.54	-0.54, 1.62	0.56	-0.90, 1.29	61	25.7	1.22	0.80, 1.88	1.15	0.72, 1.84	1.13	0.69, 1.83	36	15.2	0.87	0.53, 1.43	0.82	0.48, 1.42	0.76	0.43, 1.34
3rd Quartile	9.22	5.78	0.93	-0.15, 2.02	0.58	-0.55, 1.72	68	29.6	1.48	0.97, 2.27	1.34	0.83, 2.17	1.25	0.77, 2.05	42	18.3	1.08	0.67, 1.75	1.08	0.63, 1.88	1.01	0.58, 1.78
4th Quartile	10.16	6.14	1.86	0.79, 2.94	0.58	0.19, 2.46	91	37.9	2.16	1.43, 3.25	1.89	1.19, 3.00	1.58	0.96, 2.60	55	22.9	1.44	0.91, 2.28	1.46	0.86, 2.46	1.19	0.68, 2.09
Occupational																						
at or below median	8.42	5.58	ref		1.00	referent	82	23.6	1.00	referent	1.00	referent	1.00	referent	47	13.5	1.00	referent	1.00	referent	1.00	referent
above median	9.17	5.82	0.43	-0.10, 1.61	0.80	-0.03, 1.63	96	28.1	1.27	0.90, 1.78	1.28	0.90, 1.83	1.17	0.80, 1.70	60	17.5	1.36	0.90, 2.06	1.44	0.94, 2.22	1.22	0.78, 1.92
Sports/Exercise																						
none	9.43	6.31	ref		1.00	referent	59	31.9	1.00	referent	1.00	referent	1.00	referent	41	22.2	1.00	referent	1.00	referent	1.00	referent
at or below median	8.46	5.59	-0.97	-2.00, 0.06	-0.49	-1.51, 0.52	84	22.3	0.61	0.41, 0.91	0.70	0.47, 1.05	0.70	0.46, 1.06	52	13.8	0.56	0.36, 0.89	0.65	0.41, 1.04	0.67	0.41, 1.09
above median	9.68	5.92	0.25	-0.78, 1.28	0.58	-0.43, 1.59	126	33.4	1.07	0.74, 1.56	1.25	0.84, 1.85	1.14	0.75, 1.72	76	20.2	0.89	0.58, 1.36	1.01	0.64, 1.57	0.96	0.59, 1.54
Transportation																						
1st Quartile	8.44	5.92	ref		1.00	referent	57	25.1	1.00	referent	1.00	referent	1.00	referent	36	15.9	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	8.83	5.82	0.40	-0.67, 1.46	0.61	-0.44, 1.65	58	25.2	1.01	0.66, 1.54	1.04	0.67, 1.60	1.03	0.66, 1.63	40	17.4	1.12	0.68, 1.83	1.19	0.72, 1.97	1.25	0.74, 2.11
3rd Quartile	8.58	5.33	0.15	-0.90, 1.19	0.64	-0.38, 1.67	60	24.2	0.95	0.63, 1.45	1.12	0.73, 1.72	1.05	0.67, 1.65	36	14.5	0.90	0.55, 1.49	1.08	0.65, 1.81	1.00	0.58, 1.72
4th Quartile	10.52	6.14	2.08	1.03, 3.13	2.36	1.33, 3.38	96	39.2	1.92	1.30, 2.85	2.14	1.42, 3.21	1.67	1.06, 2.62	56	22.9	1.57	0.99, 2.50	1.73	1.08, 2.79	1.42	0.83, 2.41
Early Pregnancy##																						
Household/ caregiving																						
1st Quartile	8.74	5.94	ref		1.00	referent	29	22.8	1.00	referent	1.00	referent	1.00	referent	25	19.7	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	7.63	5.89	-1.11	-2.61, 0.38	-1.20	-2.83, 0.43	23	20.0	0.85	0.45, 1.57	0.71	0.35, 1.44	0.82	0.38, 1.81	18	15.7	0.76	0.39, 1.48	0.64	0.30, 1.38	0.74	0.32, 1.72
3rd Quartile	7.08	5.65	-1.66	-3.12, -0.21	-2.06	-3.65, -0.48	24	18.8	0.78	0.43, 1.43	0.57	0.29, 1.15	0.68	0.31, 1.46	13	10.2	0.46	0.22, 0.95	0.30	0.13, 0.71	0.33	0.13, 0.82
4th Quartile	9.28	6.27	0.54	-0.89, 1.97	-0.27	-1.92, 1.39	43	31.2	1.53	0.88, 2.65	1.10	0.56, 2.14	1.00	0.47, 2.13	35	25.4	1.39	0.78, 2.48	1.02	0.49, 2.10	1.11	0.49, 2.50
Occupational																						
at or below median	7.64	5.59	ref		1.00	referent	22	16.8	1.00	referent	1.00	referent	1.00	referent	18	13.7	1.00	referent	1.00	referent	1.00	referent
above median	7.79	6.14	0.14	-1.28, 1.57	0.27	-1.22, 1.74	29	22.5	1.44	0.78, 2.66	1.36	0.71, 2.59	0.86	0.41, 1.80	24	18.6	1.44	0.78, 2.79	1.39	0.69, 2.79	0.93	0.42, 2.03
Sports/Exercise																						
none	8.34	5.99	ref		1.00	referent	59	23.9	1.00	referent	1.00	referent	1.00	referent	45	18.2	1.00	referent	1.00	referent	1.00	referent
at or below median	8.30	6.25	-0.04	-1.28, 1.21	-0.09	-1.37, 1.19	33	23.9	1.00	0.61, 1.63	1.08	0.65, 1.80	0.94	0.53, 1.67	27	19.6	1.09	0.64, 1.86	1.25	0.72, 2.18	1.20	0.65, 2.21
above median	7.78	7.78	-0.56	-1.81, 0.68	-0.56	-1.83, 0.71	31	22.5	0.92	0.56, 1.52	0.92	0.55, 1.54	0.73	0.39, 1.34	22	15.9	0.85	0.49, 1.49	0.84	0.47, 1.51	0.62	0.31, 1.25
Transportation																						
1st Quartile	7.87	6.42	ref		1.00	referent	34	23.1	1.00	referent	1.00	referent	1.00	referent	29	19.7	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	7.74	5.28	-0.13	-1.60, 1.35	-0.11	-1.61, 1.38	23	12.1	0.89	0.49, 1.62	0.93	0.50, 1.71	0.75	0.38, 1.51	12	11.0	0.50	0.24, 1.04	0.50	0.24, 1.05	0.35	0.15, 0.81
3rd Quartile	7.77	5.72	-0.10	-1.50, 1.31	0.06	-1.37, 1.49	26	19.9	0.82	0.46, 1.46	0.93	0.52, 1.69	0.82	0.41, 1.62	20	15.3	0.73	0.39, 1.37	0.82	0.43, 1.55	0.67	0.32, 1.39
4th Quartile	9.31	6.26	1.44	0.05, 2.83	1.68	0.26, 3.10	40	29.4	1.39	0.81, 2.36	1.67	0.96, 2.89	1.37	0.71, 2.63	33	24.3	1.30	0.74, 2.29	1.53	0.85, 2.73	1.24	0.62, 2.48

Table 3.9 Odds ratios of probable depression by domain-specific physical activity level in preceding pregnancy period:Proyecto Buena Salud, 2006-2011 (continued)

	Depressive Symptoms (continuous)						At least Probable Minor Depression*								Probable Major Depression**							
			Unadjusted		Adjusted***				Unadjusted		Adjusted1***		Adjusted2****				Unadjusted		Adjusted1***		Adjusted2****	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI
Mid-Pregnancy[###]																						
Household/ caregiving																						
1st Quartile	7.42	5.31	ref		1.00	referent	23	22.8	1.00	referent	1.00	referent	1.00	referent	8	7.9	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	6.82	5.71	-0.60	-2.14, 0.95	-0.16	-1.87, 1.55	17	16.0	0.65	0.32, 1.30	0.73	0.31, 1.70	[####]		13	12.3	1.63	0.64, 4.10	2.05	0.62, 6.80	[####]	
3rd Quartile	7.11	5.70	-0.31	-1.84, 1.22	-0.23	-1.96, 1.49	20	18.0	0.75	0.38, 1.46	0.80	0.35, 1.84	[####]		17	15.3	2.10	0.87, 5.11	2.81	0.87, 9.02	[####]	
4th Quartile	7.73	6.07	0.31	-1.26, 1.88	-0.09	-1.88, 1.69	21	21.2	0.91	0.47, 1.78	0.79	0.34, 1.84	[####]		15	15.2	2.08	0.84, 5.14	2.44	0.74, 8.00	[####]	
Occupational																						
at or below median	6.34	5.22	ref		1.00	referent	13	14.1	1.00	referent	1.00	referent	1.00	referent	10	11.1	1.00	referent	1.00	referent	1.00	referent
above median	6.86	5.77	0.51	-1.04, 2.05	0.83	-0.76, 2.42	18	17.1	1.23	0.56, 2.66	1.33	0.59, 3.01	1.10	0.44, 2.77	14	13.3	1.23	0.52, 2.92	1.39	0.56, 3.45	1.33	0.45, 3.99
Sports/Exercise																						
none	6.46	5.51	ref		1.00	referent	23	15.2	1.00	referent	1.00	referent	1.00	referent	15	9.9	1.00	referent	1.00	referent	1.00	referent
at or below median	7.28	5.63	0.82	-0.50, 2.13	0.43	-0.93, 1.79	31	22.5	1.61	0.89, 2.93	1.30	0.68, 2.48	1.39	0.68, 2.84	18	13.0	1.36	0.66, 2.82	1.24	0.56, 2.73	1.42	0.58, 3.45
above median	7.97	6.05	1.51	0.17, 2.84	1.19	-0.20, 2.58	27	20.8	1.46	0.79, 2.69	1.29	0.66, 2.50	1.30	0.60, 2.79	21	16.2	1.75	0.86, 3.55	1.64	0.75, 3.57	1.90	0.77, 4.69
Transportation																						
1st Quartile	7.93	7.93	ref		1.00	referent	29	26.9	1.00	referent	1.00	referent	1.00	referent	15	13.9	1.00	referent	1.00	referent	1.00	referent
2nd Quartile	6.74	6.74	-1.19	-2.73, 0.35	-1.04	-2.61, 0.54	15	15.2	0.49	0.24, 0.98	0.48	0.23, 1.01	0.52	0.23, 1.21	12	12.1	0.86	0.38, 1.93	0.87	0.35, 2.12	1.12	0.41, 3.09
3rd Quartile	6.22	6.22	-1.70	-3.23, -0.18	-1.41	-2.97, 0.15	12	11.7	0.36	0.17, 0.75	0.40	0.19, 0.85	0.37	0.15, 0.91	6	5.8	0.38	0.14, 1.03	0.44	0.16, 1.23	0.62	0.20, 1.92
4th Quartile	7.86	7.86	-0.06	-1.55, 1.42	0.10	-1.40, 1.59	26	22.4	0.79	0.43, 1.45	0.85	0.45, 1.60	0.68	0.32, 1.48	21	18.1	1.37	0.67, 2.82	1.68	0.78, 3.63	1.44	0.57, 3.65

* EPDS score ≥13

**EPDS score ≥15

*** Household PA models adjusted for age of mother, education, live with partner or spouse, parity, BMI, smoking (prior pregnancy period), acculturation

Occupation PA models adjusted for age of mother, education, live with partner or spouse

Exercise PA models adjusted for age of mother, education, live with partner or spouse, smoking (prior pregnancy period)

Transportation PA models adjusted for age of mother, education, live with partner or spouse

****Model 2 adjustment additionally adjusted for weeks between interviews, depression in prior pregnancy period, and all other physical activity energy expenditure

[#] Examining association with early pregnancy depression

[##] Examining association with mid-to-late pregnancy depression

[###]Examining association with late pregnancy depression

[####]Model would not run

Table 3.10 Odds ratios of probable depression by intensity-specific physical activity level in same pregnancy period:Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (continuous)						At least Probable Minor Depression*						Probable Major Depression**					
			Unadjusted		Adjusted***				Unadjusted		Adjusted***				Unadjusted		Adjusted***	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Early Pregnancy																		
Light																		
1st Quartile	9.15	5.96	1.00	referent	1.00	referent	67	29.1	1.00	referent	1.00	referent	46	20	1.00	referent	1.00	referent
2nd Quartile	8.75	6.09	-0.40	-1.47, 0.67	-0.29	-1.39, 0.81	60	25.8	0.84	0.56, 1.27	0.87	0.56, 1.34	40	17.2	0.83	0.52, 1.33	0.89	0.55, 1.46
3rd Quartile	9.07	5.95	-0.08	-1.15, 0.99	0.16	-0.94, 1.26	68	29.1	1.00	0.67, 1.49	0.98	0.63, 1.52	37	15.8	0.75	0.47, 1.21	0.77	0.46, 1.29
4th Quartile	9.46	5.51	0.31	-0.76, 1.38	0.34	-0.78, 1.45	70	30.3	1.06	0.71, 1.58	0.98	0.63, 1.51	41	17.8	0.86	0.54, 1.38	0.87	0.53, 1.44
Moderate or Vigorous																		
1st Quartile	8.63	6.04	1.00	referent	1.00	referent	58	25	1.00	referent	1.00	referent			1.00	referent	1.00	referent
2nd Quartile	8.88	5.64	0.25	-0.81, 1.31	0.09	-1.00, 1.18	64	27.1	1.12	0.74, 1.68	1.04	0.67, 1.62	42	18.1	0.84	0.52, 1.37	0.87	0.52, 1.45
3rd Quartile	9.24	5.98	0.61	-0.45, 1.67	0.61	-0.50, 1.71	74	31.1	1.35	0.90, 2.03	1.29	0.83, 2.01	37	15.7	1.00	0.62, 1.60	1.06	0.64, 1.75
4th Quartile	9.72	5.83	1.09	0.02, 2.16	0.62	-0.51, 1.73	73	31.5	1.38	0.92, 2.07	1.18	0.75, 1.84	43	18.1	1.06	0.66, 1.69	1.00	0.60, 1.67
Mid-Pregnancy																		
Light																		
1st Quartile	8.76	6.19	1.00	referent	1.00	referent	51	25.8	1.00	referent	1.00	referent	41	20.7	1.00	referent	1.00	referent
2nd Quartile	8.54	6.22	-0.22	-1.41, 0.97	-0.27	-1.51, 0.97	52	26.5	1.04	0.66, 1.63	0.99	0.61, 1.61	40	20.4	0.98	0.60, 1.60	0.92	0.54, 1.55
3rd Quartile	7.55	5.75	-1.21	-2.40, -0.02	-1.42	-2.65, -0.18	40	20.2	0.73	0.46, 1.17	0.64	0.39, 1.07	30	15.2	0.68	0.41, 1.15	0.57	0.33, 1.01
4th Quartile	8.61	6.05	-0.14	-1.33, 1.04	-0.23	-1.48, 1.01	53	26.4	1.03	0.66, 1.61	0.97	0.60, 1.57	38	18.9	0.89	0.55, 1.46	0.80	0.47, 1.36
Moderate or Vigorous																		
1st Quartile	7.99	6.07	1.00	referent	1.00	referent	44	22.6	1.00	referent	1.00	referent	34	17.4	1.00	referent	1.00	referent
2nd Quartile	8.72	6.42	0.73	-0.47, 1.92	0.61	-0.63, 1.85	54	26.9	1.27	0.80, 1.99	1.19	0.73, 1.94	44	21.9	1.33	0.81, 2.19	1.26	0.74, 2.15
3rd Quartile	8.01	5.89	0.02	-1.17, 1.92	-0.09	-1.35, 1.17	43	21.4	0.93	0.58, 1.50	0.86	0.52, 1.43	29	14.4	0.80	0.47, 1.37	0.73	0.41, 1.30
4th Quartile	8.84	6	0.85	-0.34, 2.05	0.59	-0.67, 1.85	60	29.4	1.43	0.91, 2.25	1.19	0.73, 1.95	45	22.1	1.34	0.82, 2.20	1.06	0.61, 1.83
Late Pregnancy																		
Light																		
1st Quartile	7.54	5.85	1.00	referent	1.00	referent	43	22.5	1.00	referent	1.00	referent	28	14.7	1.00	referent	1.00	referent
2nd Quartile	7.53	5.66	-0.02	-0.18, 1.14	0.13	-1.08, 1.34	33	17.3	0.72	0.43, 1.19	0.74	0.43, 1.28	24	12.6	0.84	0.46, 1.50	0.90	0.47, 1.72
3rd Quartile	6.97	5.59	-0.57	-1.73, 0.59	-0.39	-1.60, 0.82	31	16.2	0.66	0.40, 1.11	0.71	0.40, 1.23	22	11.5	0.75	0.41, 1.37	0.81	0.42, 1.56
4th Quartile	7.5	6.06	-0.04	-1.20, 1.11	0.02	-1.22, 1.27	41	21.4	0.94	0.58, 1.52	0.95	0.56, 1.63	26	13.5	0.91	0.51, 1.62	0.98	0.52, 1.84
Moderate or Vigorous																		
1st Quartile	6.63	5.78	1.00	referent	1.00	referent	36	18	1.00	referent	1.00	referent	23	11.5	1.00	referent	1.00	referent
2nd Quartile	7.13	5.75	0.50	-0.64, 1.65	0.23	-0.97, 1.44	35	18.6	1.04	0.62, 1.74	0.91	0.52, 1.58	21	11.2	0.97	0.52, 1.81	0.82	0.41, 1.64
3rd Quartile	8.27	5.97	1.64	0.50, 2.78	1.61	0.42, 2.80	45	23.1	1.37	0.84, 2.23	1.19	0.71, 2.02	36	18.5	1.74	0.99, 3.07	1.75	0.95, 3.21
4th Quartile	7.58	5.61	0.93	-0.21, 2.07	0.83	-0.37, 2.03	35	18.2	1.02	0.61, 1.70	0.96	0.56, 1.65	21	10.9	0.95	0.50, 1.77	0.90	0.46, 1.75

* EPDS score ≥13

**EPDS score ≥15

*** Adjusted for maternal age, education, live with partner or spouse, generation in U.S., parity

Table 3.11 Odds ratios of probable depression by intensity-specific physical activity level in preceding pregnancy period:Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (continuous)								At least Probable Minor Depression*								Probable Major Depression**							
			Unadjusted		Adjusted1***				Unadjusted		Adjusted1***		Adjusted2****				Unadjusted		Adjusted1***		Adjusted2****			
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI		
Pre-Pregnancy																								
Light																								
1st Quartile	8.50	6.24	1.00	referent	1.00	referent	60	27.3	1.00	referent	1.00	referent	1.00	referent	36	16.4	1.00	referent	1.00	referent	1.00	referent		
2nd Quartile	8.98	5.40	0.48	-0.62, 1.58	0.77	-0.34, 1.89	55	24.6	0.87	0.57, 1.33	0.83	0.52, 1.31	0.81	0.51, 1.28	34	15.2	0.92	0.55, 1.52	1.06	0.62, 1.81	1.02	0.59, 1.76		
3rd Quartile	9.20	5.86	0.70	-0.38, 1.78	1.10	-0.01, 2.12	69	29.4	1.11	0.74, 1.67	1.22	0.78, 1.90	1.13	0.72, 1.77	45	19.2	1.21	0.75, 1.96	1.43	0.85, 2.40	1.31	0.78, 2.21		
4th Quartile	9.73	6.04	1.23	0.55, 0.14	1.62	0.52, 2.74	76	32.9	1.31	0.87, 1.96	1.37	0.89, 2.13	0.99	0.61, 1.61	47	20.4	1.31	0.81, 2.11	1.50	0.90, 2.51	1.12	0.63, 1.98		
Moderate or Vigorous																								
1st Quartile	8.29	5.81	1.00	referent	1.00	referent	48	22.4	1.00	referent	1.00	referent	1.00	referent	36	16.8	1.00	referent	1.00	referent	1.00	referent		
2nd Quartile	9.27	5.81	0.98	-0.10, 2.06	0.86	-0.25, 1.96	69	29.5	1.45	0.94, 2.22	1.41	0.90, 2.23	1.37	0.86, 2.19	46	19.7	1.21	0.75, 1.96	1.24	0.74, 2.06	1.17	0.69, 1.99		
3rd Quartile	8.77	5.68	0.48	-0.60, 1.56	0.31	-0.79, 1.42	64	27.7	1.33	0.86, 2.04	1.25	0.79, 1.98	1.13	0.70, 1.81	34	14.7	0.85	0.51, 1.42	0.91	0.53, 1.55	0.81	0.47, 1.42		
4th Quartile	10.00	6.07	1.72	0.64, 2.80	1.62	0.53, 2.72	78	32.8	1.69	1.11, 2.57	1.63	1.04, 2.54	1.37	0.84, 2.25	47	19.8	1.22	0.75, 1.97	1.26	0.76, 2.10	0.96	0.54, 1.70		
Early Pregnancy																								
Light																								
1st Quartile	8.54	6.16	1.00	referent	1.00	referent	32	25.6	1.00	referent	1.00	referent	1.00	referent	27	21.6	1.00	referent	1.00	referent	1.00	referent		
2nd Quartile	7.81	5.93	-0.74	-2.23, 0.75	-0.54	-2.10, 1.03	25	20.5	0.75	0.41, 1.36	0.78	0.41, 1.49	0.79	0.39, 1.63	15	12.3	0.51	0.26, 1.01	0.60	0.29, 1.25	0.62	0.27, 1.40		
3rd Quartile	7.12	5.89	-1.42	-2.91, 0.07	-1.21	-2.78, 0.35	22	18	0.64	0.35, 1.18	0.65	0.33, 1.26	0.64	0.31, 1.34	17	13.9	0.59	0.30, 1.14	0.63	0.30, 1.30	0.68	0.30, 1.54		
4th Quartile	9.21	5.95	0.67	-0.78, 2.12	1.01	-0.56, 2.57	40	29.4	1.21	0.70, 2.09	1.42	0.77, 2.60	1.19	0.57, 2.46	32	23.5	1.12	0.62, 2.00	1.44	0.75, 2.75	1.38	0.63, 3.02		
Moderate or Vigorous																								
1st Quartile	8.34	6.00	1.00	referent	1.00	referent	30	22.7	1.00	referent	1.00	referent	1.00	referent	24	18.2	1.00	referent	1.00	referent	1.00	referent		
2nd Quartile	7.87	5.88	-0.47	-1.95, 1.00	-0.60	-2.17, 0.97	24	19.5	0.82	0.45, 1.51	0.87	0.45, 1.67	0.70	0.34, 1.48	18	14.6	0.77	0.40, 1.50	0.82	0.40, 1.67	0.67	0.30, 1.50		
3rd Quartile	8.04	6.08	-0.30	-1.76, 1.15	-0.29	-1.86, 1.27	30	23.1	1.02	0.57, 1.82	0.99	0.52, 1.88	0.79	0.39, 1.61	22	16.9	0.92	0.49, 1.73	0.92	0.46, 1.87	0.69	0.31, 1.50		
4th Quartile	8.78	6.15	0.43	-1.03, 1.89	0.24	-1.41, 1.77	39	30.5	1.49	0.86, 2.59	1.46	0.78, 2.73	1.07	0.50, 2.30	30	23.4	1.38	0.75, 2.52	1.36	0.69, 2.70	1.01	0.43, 2.35		
Mid- Pregnancy																								
Light																								
1st Quartile	7.04	5.64	1.00	referent	1.00	referent	18	17.7	1.00	referent	1.00	referent	1.00	referent	7	6.9	1.00	referent	1.00	referent	1.00	referent		
2nd Quartile	7.38	5.61	0.70	-0.87, 2.26	0.18	-1.51, 1.86	25	24.3	1.50	0.76, 2.95	1.07	0.49, 2.32	0.72	0.30, 1.72	17	16.5	2.68	1.06, 6.78	1.71	0.61, 4.81	1.70	0.53, 5.40		
3rd Quartile	6.72	5.51	-0.33	-1.89, 1.24	-0.64	-2.35, 1.06	15	14.7	0.81	0.38, 1.70	0.64	0.28, 1.47	0.48	0.19, 1.25	12	11.8	1.81	0.68, 4.80	1.41	0.50, 4.04	2.03	0.63, 6.58		
4th Quartile	7.38	6.19	0.34	-1.23, 1.92	0.42	-1.25, 2.09	21	21	1.24	0.62, 2.50	1.18	0.55, 2.53	0.71	0.29, 1.77	17	17	2.78	1.1, 7.03	2.46	0.93, 6.56	2.52	0.81, 7.83		
Moderate or Vigorous																								
1st Quartile	6.95	5.62	1.00	referent	1.00	referent	20	19.6	1.00	referent	1.00	referent	1.00	referent	11	10.8	1.00	referent	1.00	referent	1.00	referent		
2nd Quartile	7.12	5.54	0.17	-1.46, 1.80	-0.10	-1.85, 1.64	18	19.6	1.00	0.49, 2.03	0.80	0.36, 1.80	0.54	0.21, 1.37	11	12	1.12	0.46, 2.73	0.80	0.29, 2.24	0.62	0.19, 2.05		
3rd Quartile	7.25	5.80	0.29	-1.28, 1.86	0.05	-1.67, 1.77	19	17.9	0.90	0.45, 1.80	0.81	0.37, 1.78	0.51	0.20, 1.28	15	14.2	1.36	0.59, 3.13	1.09	0.42, 2.83	1.10	0.37, 3.31		
4th Quartile	7.51	6.18	0.56	-1.01, 2.13	0.55	-1.14, 2.25	21	19.8	1.01	0.51, 2.01	1.02	0.47, 2.18	0.74	0.29, 1.88	17	16	1.58	0.70, 3.56	1.62	0.65, 4.04	1.5	0.50, 4.56		

* EPDS score ≥13

**EPDS score ≥15

*** Model 1 Adjusted for maternal age, education, live with partner or spouse, generation in U.S., parity, weeks between interviews

****Model 2 adjustment additionally adjusted for depressive symptoms in prior pregnancy period and all other physical activity expenditure

Table 3.12 Odds ratios of probable depression by whether participant met ACOG Physical Activity Guidelines:Proyecto Buena Salud, 2006-2011[#]

	Depressive Symptoms (continuous)						At least Probable Minor Depression*								Probable Major Depression**							
			Unadjusted		Adjusted1***				Unadjusted		Adjusted1***		Adjusted2****				Unadjusted		Adjusted1***		Adjusted2****	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI
Physical Activity in Same Pregnancy Period																						
Early Pregnancy PA																						
Met ACOG Guidelines - All Activity																						
No	9.49	6.29	1.00	referent	1.00	referent	47	25.0	1.00	referent	1.00	referent	n/a	n/a	40	21.3	1.00	referent	1.00	referent	n/a	n/a
Yes	9.27	5.76	0.77	-0.16,1.71	0.51	-0.46, 1.48	227	29.3	1.24	0.86, 1.79	1.16	0.78, 1.73			131	16.9	0.75	0.51, 1.12	0.74	0.48, 1.14		
Met ACOG Guidelines - Only Exercise																						
No	8.99	5.85	1.00	referent	1.00	referent	174	27.2	1.00	referent	1.00	referent	n/a	n/a	109	17.0	1.00	referent	1.00	referent	n/a	n/a
Yes	9.36	5.93	0.36	-0.43,1.15	0.30	-0.51, 1.11	100	31.3	1.22	0.91, 1.64	1.20	0.98, 1.64			62	19.4	1.17	0.83, 1.66	1.15	0.79, 1.65		
Mid Pregnancy PA																						
Met ACOG Guidelines - All Activity																						
No	7.88	6.36	1.00	referent	1.00	referent	31	21.5	1.00	referent	1.00	referent	n/a	n/a	26	18.1	1.00	referent	1.00	referent	n/a	n/a
Yes	8.47	6.05	0.59	-0.51,1.69	0.42	-0.75, 1.59	172	25.7	1.26	0.82, 1.94	1.18	0.73, 1.91			127	19.0	1.06	0.67, 1.69	0.95	0.56, 1.59		
Met ACOG Guidelines - Only Exercise																						
No	8.4	6.27	1.00	referent	1.00	referent	136	26.3	1.00	referent	1.00	referent	n/a	n/a	104	20.1	1.00	referent	1.00	referent	n/a	n/a
Yes	8.34	5.81	-0.06	-0.93, 0.81	-0.08	-0.97, 0.81	67	22.7	0.83	0.59, 1.15	0.81	0.57, 1.14			49	16.6	0.79	0.55, 1.15	0.75	0.50, 1.11		
Late Pregnancy PA																						
Met ACOG Guidelines - All Activity																						
No	7.05	5.94	1.00	referent	1.00	referent	33	21.3	1.00	referent	1.00	referent	n/a	n/a	21	13.6	1.00	referent	1.00	referent	n/a	n/a
Yes	7.47	5.75	0.42	-0.60, 1.43	0.41	-0.66, 1.47	120	18.9	0.86	0.56, 1.33	0.79	0.50, 1.25			82	12.9	0.94	0.56, 1.58	0.94	0.54, 1.64		
Met ACOG Guidelines - Only Exercise																						
No	7.08	5.67	1.00	referent	1.00	referent	93	19.1	1.00	referent	1.00	referent	n/a	n/a	55	11.3	1.00	referent	1.00	referent	n/a	n/a
Yes	7.92	7.91	0.83	0.00, 1.66	0.88	0.002, 1.76	60	19.9	1.06	0.74, 1.52	1.08	0.73, 1.60			48	16.0	1.49	0.98, 2.27	1.62	1.03, 2.55		
Physical Activity in Previous Pregnancy Period																						
Early Pregnancy PA[#]																						
Met ACOG Guidelines - All Activity																						
No	7.94	6.11	1.00	referent	1.00	referent	23	23.0	1.00	referent	1.00	referent	1.00	referent	18	18.0	1.00	referent	1.00	referent	1.00	referent
Yes	8.23	5.97	0.29	-1.01, 1.60	0.09	-1.34, 1.53	100	23.5	1.03	0.61, 1.73	0.95	0.52, 1.73	0.89	0.46, 1.70	76	17.9	0.95	0.49, 1.82	0.94	0.49, 1.80	0.96	0.47, 1.94
Met ACOG Guidelines - Only Exercise																						
No	8.25	6.01	1.00	referent	1.00	referent	86	23.8	1.00	referent	1.00	referent	1.00	referent	66	18.3	1.00	referent	1.00	referent	1.00	referent
Yes	8.04	5.98	-0.21	-1.3, 0.91	-0.21	-1.36, 0.95	37	22.8	0.83	0.59,1.15	0.96	0.60, 1.52	0.90	0.54, 1.51	28	17.3	0.95	0.57, 1.59	0.95	0.57, 1.59	0.91	0.52, 1.61

Table 3.12 Odds ratios of probable depression by whether participant met ACOG Physical Activity Guidelines:Proyecto Buena Salud, 2006-2011[#] (continued)

	Depressive Symptoms (continuous)						At least Probable Minor Depression*								Probable Major Depression**							
			Unadjusted		Adjusted1***				Unadjusted		Adjusted1***		Adjusted2****				Unadjusted		Adjusted1***		Adjusted2****	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI	OR	95%CI
Mid Pregnancy PA[##]																						
Met ACOG Guidelines - All Activity																						
No	7.16	5.46	1.00	referent	1.00	referent	19	22.4	1.00	referent	1.00	referent	1.00	referent	8	9.4	1.00	referent	1.00	referent	1.00	referent
Yes	7.21	5.81	0.04	-1.32, 1.41	0.09	-1.62, 1.43	62	18.5	0.79	0.44, 1.41	0.70	0.36, 1.37	0.57	0.26, 1.21	46	13.7	1.53	0.69, 3.39	1.46	0.57, 3.74	1.64	0.57, 4.76
Met ACOG Guidelines - Only Exercise																						
No	6.88	5.62	1.00	referent	1.00	referent	50	18.7	1.00	referent	1.00	referent	1.00	referent	30	11.2	1.00	referent	1.00	referent	1.00	referent
Yes	7.75	7.75	0.87	-0.28, 2.02	0.99	-0.20, 2.18	31	20.5	1.13	0.68, 1.86	1.20	0.69, 2.02	1.19	0.65, 2.17	24	15.9	1.50	0.84, 2.67	1.65	0.88, 3.08	1.97	0.94, 4.12

* EPDS score ≥13

**EPDS score ≥15

*** Adjusted for maternal age, education, live with partner or spouse, generation in U.S., parity, weeks between interviews

****Model 1 additionally adjusted for depressive symptoms in prior pregnancy period

[#] Examining association with mid-pregnancy depression

[##] Examining association with late pregnancy depression

Table 3.13 Odds ratios of probable depression in mid and late pregnancy by physical activity during preceding pregnancy period among women that were not depressed in previous period: Proyecto Buena Salud, 2006-2011

	Depressive Symptoms (continuous)						At least Probable Minor Depression*						Probable Major Depression**					
			Unadjusted		Adjusted***				Unadjusted		Adjusted***				Unadjusted		Adjusted***	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Early Pregnancy PA#																		
Total Physical Activity																		
1st Quartile	6.81	5.46	1.00	referent	1.00	referent	14	15.1	1.00	referent	1.00	referent	11	11.8	1.00	referent	1.00	referent
2nd Quartile	6.06	4.52	-0.75	-2.28, 0.79	-0.82	-2.36, 0.72	8	9.8	0.61	0.24, 1.54	0.55	0.21, 1.43	3	3.7	0.28	0.08, 1.05	0.25	0.06, 0.96
3rd Quartile	6.59	4.72	-0.22	-1.66, 1.22	-0.21	-1.67, 1.25	12	11.5	0.74	0.32, 1.68	0.79	0.34, 1.84	7	6.7	0.54	0.20, 1.45	0.56	0.20, 1.57
4th Quartile	7.00	5.96	0.19	-1.32, 1.71	0.04	-1.50, 1.59	15	18.8	1.31	0.60, 2.87	1.35	0.59, 3.07	13	15.3	1.35	0.57, 3.19	1.53	0.62, 3.76
Met ACOG Guidelines - All Activity																		
No	6.21	4.67	1.00	referent	1.00	referent	9	12.0	1.00	referent	1.00	referent	6	8.0	1.00	referent	1.00	referent
Yes	6.70	5.26	0.49	0.81, 1.78	0.50	-0.82, 1.82	44	14.2	1.21	0.56, 2.60	1.37	0.61, 3.06	30	9.7	1.23	0.49, 3.07	1.50	0.57, 3.96
Met ACOG Guidelines - Only Exercise																		
No	6.89	5.25	1.00	referent	1.00	referent	41	15.1	1.00	referent	1.00	referent	28	10.3	1.00	referent	1.00	referent
Yes	5.92	4.87	-0.97	-2.10, 0.16	-0.92	-2.06, 0.22	12	10.6	0.67	0.34, 1.32	0.68	0.34, 1.37	8	7.1	0.66	0.29, 1.50	0.65	0.28, 1.50
Intensity of Physical Activity																		
Light																		
1st Quartile	6.79	5.19	1.00	referent	1.00	referent	14	15.6	1.00	referent	1.00	referent	11	12.2	1.00	referent	1.00	referent
2nd Quartile	6.38	4.86	-0.41	-1.88, 1.06	-0.65	-2.17, 0.87	11	11.8	0.73	0.31, 1.70	0.58	0.24, 1.39	4	4.3	0.32	0.10, 1.06	0.24	0.07, 0.82
3rd Quartile	5.56	4.73	-1.23	-2.70, 1.06	-1.44	-2.96, 0.08	8	8.6	0.51	0.20, 1.29	0.41	0.16, 1.07	5	5.4	0.41	0.14, 1.23	0.33	0.11, 1.01
4th Quartile	7.65	5.62	0.86	-0.61, 2.33	0.56	-1.06, 2.18	17	18.1	1.20	0.55, 2.60	0.98	0.41, 2.32	14	14.9	1.26	0.54, 2.94	1.10	0.42, 2.84
Moderate or Vigorous																		
1st Q	7.00	5.18	1.00	referent	1.00	referent	14	14.0	1.00	referent	1.00	referent	11	11.0	1.00	referent	1.00	referent
2nd Q	6.46	5.16	-0.54	-2.02, 0.93	-0.71	-2.22, 0.80	11	12.2	0.86	0.37, 2.00	0.83	0.33, 2.05	7	7.8	0.68	0.25, 1.84	0.61	0.21, 1.81
3rd Q	6.27	4.84	-0.73	-2.19, 0.73	-0.85	-2.37, 0.67	11	11.8	0.82	0.35, 1.92	0.83	0.33, 2.05	5	5.4	0.46	0.15, 1.38	0.48	0.15, 1.50
4th Q	6.94	5.64	-0.06	-1.53, 1.41	-0.58	-2.20, 1.04	17	18.7	1.41	0.65, 3.06	1.31	0.54, 3.17	13	14.3	1.35	0.57, 3.18	1.21	0.45, 3.27
Type of Physical Activity																		
Household																		
1st Quartile	7.16	5.11	1.00	referent	1.00	referent	12	13.2	1.00	referent	1.00	referent	10	11.0	1.00	referent	1.00	referent
2nd Quartile	6.37	5.02	-0.79	-2.27, 0.68	-0.71	-2.23, 0.81	12	13.0	0.99	0.42, 2.33	1.24	0.50, 3.06	8	8.7	0.77	0.29, 2.05	0.94	0.33, 2.67
3rd Quartile	5.62	4.51	-1.55	-2.99, '-0.10	-1.56	-3.07, '-0.05	10	10.1	0.74	0.30, 1.81	0.84	0.33, 2.14	3	3.0	0.25	0.07, 0.95	0.26	0.07, 1.02
4th Quartile	7.45	5.74	0.29	-1.19, 1.76	0.15	-1.42, 1.72	16	17.6	1.40	0.62, 3.17	1.75	0.72, 4.26	13	14.3	1.35	0.56, 3.26	1.71	0.64, 4.55

Table 3.13 Odds ratios of probable depression in mid and late pregnancy by physical activity during preceding pregnancy period among women that were not depressed in previous period: Proyecto Buena Salud, 2006-2011 (continued)

	Depressive Symptoms (continuous)						At least Probable Minor Depression*						Probable Major Depression**					
			Unadjusted		Adjusted***				Unadjusted		Adjusted***				Unadjusted		Adjusted***	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Occupational																		
At or below median	6.43	4.77	1.00	referent	1.00	referent	10	9.4	1.00	referent	1.00	referent	7	6.6	1.00	referent	1.00	referent
Above median	6.49	5.57	0.06	-1.35, 1.48	-0.28	-1.77, 1.21	16	16.3	1.87	0.81, 4.35	1.59	0.62, 4.10	12	12.2	1.97	0.74, 5.25	1.89	0.63, 5.64
Transportation																		
1st Quartile	6.29	5.35	1.00	referent	1.00	referent	15	13.4	1.00	referent	1.00	referent	10	8.9	1.00	referent	1.00	referent
2nd Quartile	6.79	5.07	0.50	-0.97, 1.98	0.39	-1.15, 1.92	12	14.8	1.13	0.50, 2.55	0.92	0.37, 2.26	8	9.9	1.12	0.42, 2.97	0.96	0.35, 2.64
3rd Quartile	6.59	5.19	0.30	-1.08, 1.69	0.09	-1.35, 1.54	14	13.7	1.03	0.47, 2.25	0.94	0.40, 2.21	11	10.8	1.23	0.50, 3.04	1.31	0.51, 3.34
4th Quartile	6.89	5.03	0.60	-0.83, 2.03	0.59	-0.99, 2.16	12	13.3	1.00	0.44, 2.25	1.02	0.41, 2.55	7	7.8	0.86	0.31, 2.36	1.10	0.39, 3.11
Exercise																		
None	7.06	5.39	1.00	referent	1.00	referent	29	15.6	1.00	referent	1.00	referent	22	11.8	1.00	referent	1.00	referent
At or below median	6.47	5.00	-0.60	-1.84, 0.65	-1.21	-2.52, 0.11	13	13.0	0.81	0.40, 1.64	0.59	0.27, 1.32	7	7.0	0.56	0.23, 1.36	0.39	0.14, 1.10
Above median	5.88	4.80	-1.19	-2.4, 0.07	-1.51	-2.85, -0.17	11	11.2	0.69	0.33, 1.44	0.51	0.23, 1.15	7	7.1	0.57	0.24, 1.39	0.36	0.13, 0.96
Mid- Pregnancy PA [##]																		
Total Physical Activity																		
1st Quartile	5.80	4.99	1.00	referent	1.00	referent	11	13.8	1.00	referent	1.00	referent	4	5.0	1.00	referent	1.00	referent
2nd Quartile	6.13	5.02	0.33	-1.26, 1.91	0.46	-1.18, 2.09	9	12.5	0.90	0.35, 2.31	0.96	0.34, 2.71	5	6.9	1.42	0.37, 5.50	1.44	0.30, 6.85
3rd Quartile	5.31	4.86	-0.49	-2.05, 1.06	-0.11	-1.73, 1.51	8	10.3	0.72	0.27, 1.89	0.86	0.31, 2.44	6	7.7	1.58	0.43, 5.84	2.04	0.48, 8.76
4th Quartile	5.91	5.20	0.11	-1.44, 1.66	0.28	-1.31, 1.85	9	11.4	0.81	0.32, 2.07	0.92	0.34, 2.50	8	10.1	2.14	0.62, 7.42	2.68	0.67, 10.75
Met ACOG Guidelines - All Activity																		
No	6.50	5.07	1.00	referent	1.00	referent	13	18.6	1.00	referent	1.00	referent	5	7.1	1.00	referent	1.00	referent
Yes	5.62	4.93	-0.88	-2.19, 0.43	-0.70	-2.02, 0.63	27	10.6	0.52	0.25, 1.07	0.59	0.27, 1.27	18	7.0	0.98	0.35, 2.75	1.16	0.37, 3.62
Met ACOG Guidelines - Only Exercise																		
No	5.59	5.01	1.00	referent	1.00	referent	28	13.6	1.00	referent	1.00	referent	13	6.3	1.00	referent	1.00	referent
Yes	6.18	4.90	0.59	-0.53, 1.71	0.52	-0.62, 1.64	12	10.1	0.71	0.35, 1.46	0.68	0.32,1.44	10	8.4	1.36	0.58, 3.21	1.31	0.53, 3.22
Intensity of Physical Activity																		
Light																		
1st Quartile	5.63	4.74	1.00	referent	1.00	referent	8	9.9	1.00	referent	1.00	referent	2	2.5	1.00	referent	1.00	referent
2nd Quartile	6.49	5.31	0.86	-0.71, 2.43	0.61	-1.05, 2.27	14	19.2	2.17	0.85, 5.51	2.11	0.74, 6.07	8	11.0	3.55	0.69, 18.23	3.96	0.74, 21.25
3rd Quartile	5.52	4.74	-0.11	-1.62, 1.40	-0.20	-1.82, 1.42	7	8.2	0.82	0.28, 2.37	0.86	0.27, 2.77	5	5.9	2.40	0.45, 12.75	2.17	0.38, 12.45
4th Quartile	5.81	5.21	0.18	-1.37, 1.72	-0.13	-1.85, 1.58	10	12.8	1.34	0.50, 3.60	1.03	0.32, 3.28	8	10.3	2.18	0.62, 16.29	3.27	0.60, 17.66

Table 3.13 Odds ratios of probable depression in mid and late pregnancy by physical activity during preceding pregnancy period among women that were not depressed in previous period: Proyecto Buena Salud, 2006-2011 (continued)

	Depressive Symptoms (continuous)						At least Probable Minor Depression*						Probable Major Depression**					
			Unadjusted		Adjusted***				Unadjusted		Adjusted***				Unadjusted		Adjusted***	
	mean	SD	Beta	95%CI	Beta	95%CI	n	%	OR	95%CI	OR	95%CI	n	%	OR	95%CI	OR	95%CI
Moderate or Vigourous																		
1st Quartile	6.04	5.08	1.00	referent	1.00	referent	12	14.1	1.00	referent	1.00	referent	6	7.1	1.00	referent	1.00	referent
2nd Quartile	5.58	5.13	-0.46	-1.88, 1.13	-0.04	-1.71, 1.63	9	13.6	0.96	0.38, 2.44	1.30	0.48, 3.49	5	7.6	1.08	0.32, 3.70	1.36	0.36, 5.09
3rd Quartile	5.66	4.75	-0.37	-1.88, 1.13	-0.14	-1.71, 1.42	8	9.6	0.65	0.25, 1.68	0.65	0.23, 1.87	5	6.0	0.84	0.25, 2.88	0.65	0.16, 2.67
4th Quartile	5.71	5.09	-0.33	-1.85, 1.20	-0.02	-1.72, 1.68	8	10.1	0.69	0.26, 1.78	0.70	0.23, 2.12	7	8.9	1.28	0.41, 3.99	0.92	0.24, 3.54
Type of Physical Activity																		
Household																		
1st Quartile	6.80	5.10	1.00	referent	1.00	referent	17	19.5	1.00	referent	1.00	referent	5	5.8	1.00	referent	1.00	referent
2nd Quartile	5.92	4.95	-0.89	-2.36, 0.59	-0.73	-2.31, 0.84	9	10.7	0.49	0.21, 1.18	0.57	0.21, 1.50	7	8.3	1.49	0.45, 4.90	1.22	0.34, 4.36
3rd Quartile	4.90	4.46	-1.91	-3.40, '0.41	-1.87	-3.46, -0.27	6	7.6	0.34	0.13, 0.91	0.29	0.09, 0.94	4	5.1	0.88	0.23, 3.38	0.64	0.15, 2.87
4th Quartile	5.91	5.27	-0.90	-2.43, 0.63	-0.82	-2.45, 0.82	9	12.2	0.57	0.24, 1.37	0.62	0.23, 1.67	7	9.5	1.71	0.52, 5.64	1.26	0.35, 4.45
Occupational																		
At or below median	5.32	4.46	1.00	referent	1.00	referent	6	7.8	1.00	referent	1.00	referent	4	5.2	1.00	referent	1.00	referent
Above median	6.08	5.38	0.76	-0.76, 2.28	0.65	-0.97, 2.27	12	14.0	1.92	0.68, 5.39	1.64	0.55, 4.94	9	10.5	2.13	0.63, 7.23	1.43	0.38, 5.34
Transportation																		
1st Quartile	7.26	6.15	1.00	referent	1.00	referent	14	17.3	1.00	referent	1.00	referent	5	6.2	1.00	referent	1.00	referent
2nd Quartile	6.32	5.55	-0.98	-2.49, 0.54	-0.80	-2.42, 0.83	7	8.6	0.45	0.17, 1.19	0.49	0.17, 1.46	5	6.2	1.00	0.28, 3.60	0.89	0.21, 3.84
3rd Quartile	6.82	5.18	-1.17	-2.67, 0.32	-0.77	-2.42, 0.88	6	7.1	0.36	0.13, 0.99	0.39	0.12, 1.25	2	2.4	0.37	0.07, 1.94	0.38	0.07, 2.24
4th Quartile	6.74	5.23	0.03	-1.48, 1.53	0.17	-1.51, 1.84	14	16.9	0.97	0.43, 2.19	0.99	0.37, 2.66	11	13.3	2.32	0.77, 7.01	2.03	0.55, 7.44
Exercise																		
None	5.22	4.94	1.00	referent	1.00	referent	12	10.3	1.00	referent	1.00	referent	8	6.9	1.00	referent	1.00	referent
At or below median	5.93	4.98	0.71	-0.59, 2.01	0.85	-0.51, 2.20	18	17.0	1.77	0.81, 3.88	1.87	0.79, 4.39	7	6.6	0.96	0.33, 2.73	1.05	0.35, 3.19
Above median	6.32	4.97	1.10	-0.21, 2.41	0.15	-0.29,2.58	10	9.7	0.93	0.39, 2.26	0.76	0.27, 2.13	8	7.8	1.14	0.41, 3.15	0.85	0.26, 2.71

* EPDS score ≥13

**EPDS score ≥15

[#] Examining association with mid-pregnancy depression

[##]Examining association with late pregnancy depression

***Adjusted age, education, live with partner or spouse, all other forms of energy expenditure, weeks between interviews, all other forms of energy expenditure (domain and intensity specific physical activity only)

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