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Economic perturbations and fetal growth: A multilevel analysis of exposure to labor market insecurity during gestation and birth weight for gestational age

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Economic perturbations and fetal growth: A multilevel analysis of exposure to labor market insecurity during gestation and birth weight for gestational age

By

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Abstract

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by

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Doctor of Philosophy in Epidemiology

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Background. Epidemiologic research has made important strides in identifying individual-level risk factors for adverse birth outcomes such as low birth weight and preterm birth, which carry high clinical, social, and economic costs. Despite this accumulated knowledge, we remain unable to explain differences in the distribution of birth outcomes between populations and within populations across space and time, suggesting the need to consider macro-level, ecologic determinants of birth outcomes. In this dissertation, I developed a conceptual model based on ecologic and evolutionary theory and research that proposes that unexpected changes to the human ecology, i.e. perturbations, may result in unexpected behavioral and biological responses in humans and that such responses will be conserved by natural selection if they are adaptive. Based on this framework, I hypothesized that reductions in fetal growth would occur in response to maternal exposure to ecological perturbations—specifically, perturbations to labor market security—during gestation.

Methods. I examined the association between maternal exposure to state-level labor market perturbations during each trimester of gestation and fetal growth, as measured by birth weight for gestational age percentile. The study population included 6,715 gestations and births between 1982 and 2000 to women enrolled in the National Longitudinal Survey of Youth 1979 (NLSY79). I calculated birth weight for gestational age percentiles using national reference data and categorized births $<10^{th}$ percentile as small for gestational age (SGA).

I defined perturbations to labor market security as months in which the state unemployment rate was higher than its statistically expected value (i.e., unexpectedly high labor market insecurity) and months in which the state unemployment rate was lower than its statistically expected value (i.e., unexpectedly high security). I derived statistically expected values using ARIMA modeling methods to account for autocorrelation. Gestations in the NLSY79 were classified as either exposed or unexposed to labor market insecurity or security in the first, second, and third trimester if one of these labor market perturbations occurred in the maternal state of residence during that trimester.

I used linear and logistic regression models to examine the association between labor market perturbations in each trimester and birth weight percentile and odds of SGA. I also examined whether any observed associations differed by maternal race/ethnicity, childhood socioeconomic status, educational attainment, marital status, employment status, or poverty status. Finally, I explored whether any observed associations were mediated by individual economic change (i.e., changes in maternal employment status or household income) or maternal pregnancy behaviors (i.e., smoking, first trimester utilization of prenatal care, or net gestational

weight gain). If associations were mediated by one these factors, I calculated the proportion of the total association explained by that factor.

Results. Exposure to labor market insecurity in the first trimester was significantly associated with a decrease in birth weight for gestational age of 4.05 percentile points (95% CI = -6.87, -1.22) and higher odds of SGA (OR = 1.50, 95% CI = 1.21, 1.86). Exposure to labor market insecurity in the second and third trimesters was not significantly associated with either outcome. Exposure to labor market security was not associated with birth weight for gestational age percentile or SGA.

The association between exposure to labor market insecurity in the first trimester and birth weight percentile differed significantly by maternal childhood SES, educational attainment, and employment status but not by race/ethnicity, marital status, or poverty status. Exposure to labor market insecurity in the first trimester was associated with decreases in birth weight percentile of 5.52 (95% CI = -10.0, -1.04) and 8.66 points (95% CI = -14.04, -3.29) among women with average or high childhood SES, respectively, while the association was not significant among women with low childhood SES. Exposure to labor market insecurity in the first trimester was associated with a decrease in birth weight percentile of 9.22 points (95% CI = -15.77, -2.88) among women with <12 years educational attainment, while the association was not significant among women with 12 years or >12 years educational attainment. Exposure to labor market insecurity was associated with a decrease in birth weight percentile of 7.10 points (95% CI = -12.33, -1.87) and 10.27 points (95% CI = (-18.82, -1.71) among women keeping house and out of the labor force, respectively, while the association was not significant among employed and unemployed women.

My exploration of mediation by individual economic change and maternal pregnancy behaviors found that approximately 11% of the association between exposure to labor market insecurity in the first trimester and birth weight percentile was explained by net maternal gestational weight gain. The association also differed significantly by maternal smoking, with the association only significant among smokers. No other individual economic change or maternal pregnancy behaviors mediated greater than one percent of the association.

Conclusions. Findings support my hypothesis that fetal growth responds to a contemporary ecological perturbation, i.e., unexpectedly high labor market insecurity. Exposure to this perturbation appears to have more impact on fetal growth if it occurs in the first trimester of gestation. The finding that associations between exposure to labor market insecurity and birth weight percentile were stronger among women with high childhood SES, <12 years education, and those keeping house or out of the labor force suggests that these women may be more vulnerable to economic perturbations. Although further research on mediation is needed, initial findings suggest that maternal gestational weight gain may represent one pathway through which economic perturbations affect fetal growth.

This dissertation is dedicated to my husband, Stephen Zilko, who moved across the country to enable me to pursue a graduate education; who has provided unfailing love and support (both emotional and logistical) for the past five years; who has encouraged me through my uncertainties and celebrated my successes; and who has never let me forget to laugh.

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Chapter I: Introduction and theoretical framework

Introduction

Measures of gestational health such as birth weight and preterm birth consistently differ between populations defined by race [1,2], geography[3], and socioeconomic status[2] in the United States. Black women, for example, have higher rates of preterm birth and low birth weight (LBW, <2500 g) than Hispanics, Asian/Pacific Islanders (API), and non-Hispanic whites , yet foreign-born black women have lower rates than black women born in the U.S.[1,4,5] Birth outcomes also exhibit unexplained temporal trends both within and between populations. Rates of LBW and preterm birth increased dramatically between the 1980s and 2006, but the rate of increase varied substantially by race/ethnicity.[3] Examining the determinants of these between- and within-population differences in birth outcomes represents a critical line of inquiry, especially in light of increasing evidence that gestational health predicts later-life health.[6] Epidemiologic research has traditionally focused on identifying individual-level determinants of birth outcomes. After decades of such research, however, identified individual-level factors—e.g. maternal diet, smoking, and age—leave much of the between-population and temporal variation in birth weight outcomes unexplained.[1,7]

In this chapter, I first describe the epidemiology of birth outcomes, including these enduring between- and within-population differences. I then describe a conceptual framework based on ecologic and evolutionary principles and theory that I propose can help inform research on birth outcomes and potentially shed light on some of these unexplained population-level differences and trends. I draw on ecologic theory to describe how aspects of human behavior and biology respond to perturbations in the human ecosystem, and I use evolutionary theory to suggest potential adaptive responses to ecologic perturbations that may occur during human reproduction. Based on this ecological-evolutionary framework, I develop the primary research question of my dissertation, which seeks to understand how perturbations to an important contemporary ecological factor—labor market security—may affect fetal growth.

Epidemiology of birth weight outcomes

Gestation represents a complex process encompassing conception, implantation of the embryo, development of the placenta, the processes of fetal growth and development, and (often) delivery of a live infant. Much about the determinants and mechanisms of these processes remains unknown, however, due to our inability to measure or experiment on many aspects of human gestation. Researchers therefore often utilize data on birth weight and length of gestation (hereafter referred to as birth outcomes) as proxy measures of the overall health or success of gestation. These variables are routinely collected at birth and recorded on birth certificates, and are also often self-reported in large survey data.

<u>Associations between birth outcomes and mortality and morbidity.</u> Epidemiologic and clinical evidence that birth weights and lengths of gestation outside of well-defined ranges are associated with increased risk of neonatal and infant morbidity and mortality has lead to the definition of “adverse” birth outcomes. Infants weighing less than 2500 g at birth are considered low birth weight (LBW), those weighing less than 1500 g are considered very low birth weight

(VLBW), and those weighing greater than 4000 g are classified as having "macrosomia". Because infants born early are necessarily smaller, birth weight for gestational age percentiles, which derive from national distributions of birth weights at each gestational age, represent a better approximation of fetal growth than birth weight alone.[8] Small for gestational age (SGA) describes infants less than the 10^{th} percentile of weight for gestational age while large for gestational age (LGA) describes those greater than the 90^{th} percentile. Low weight or SGA birth is associated with increased risk of neonatal and infant mortality, respiratory distress syndrome (RDS), intraventricular hemorrhage, cardiovascular and intestinal abnormalities, and vision problems.[9] Macrosomia and LGA are associated with prolonged labor and complications of labor and delivery.[10]

Deliveries at or before 37 completed weeks gestation are classified as "preterm", those at or before 34 completed weeks are considered "very preterm", and those after 42 weeks are "postterm". Preterm birth is associated with increased risk of neonatal and infant mortality, RDS, intestinal injury, compromised immune function, and neurological, cardiovascular, hearing and vision problems.[1] Postterm delivery is associated with a smaller (relative to preterm) increase in risk of infant mortality as well as increased risk of low Apgar score, fetal distress, labor and delivery complications, and admission to the neonatal intensive care unit.[11]

Seminal studies published by Barker and colleagues in 1989 reported that birth weight was inversely associated with later life blood pressure and rates of ischemic heart disease.[12,13] A growing body of literature has since reported associations between birth weight and later-life health outcomes such as obesity, diabetes, and mental health [14-16]. Small and preterm infants also reportedly have lower educational attainment and adult income compared to normal weight and term infants, respectively.[17,18] It remains a subject of much debate whether these associations between birth weight and length of gestation and early-life and later-life outcomes indicate a causal effect of birth outcomes on subsequent health or, rather, reflect some underlying aspect of the gestational process that affects both birth and later-life outcomes.

Individual-level factors associated with birth outcomes. The substantial personal, medical, and societal costs associated with adverse birth outcomes have generated much research interest in identifying causes. A large body of clinical and epidemiologic literature has identified clusters of individual-level risk factors associated with low birth weight[19] and preterm birth[1], including maternal age, genetics, parity, pregnancy health (e.g. diabetes, infection, high or low body mass index (BMI), chronic hypertension and pregnancy hypertensive disorders); psychosocial status (self-reported stress, social support), behaviors (e.g. drug use, physical activity, sleep, smoking, diet, pre-pregnancy weight and pregnancy weight gain); and environmental exposures.

Between- and within-population differences in birth outcomes. Despite the identification of many individual-level risk factors, much of the between-population and temporal variation in birth outcomes at the population level remains unexplained. Distributions of birth outcomes vary between populations defined by maternal socioeconomic status (e.g., education and income), race/ethnicity, country of origin, and neighborhood or state of residence.[1,5,11] Women of low individual-level socioeconomic status (SES, i.e., income or education) as well as those living in neighborhoods characterized by poverty, unemployment, or high crime rates exhibit higher rates of preterm delivery and LBW.[1,19,20] In 2006, 11.9% of births among non-Hispanic black women were LBW, while only 4.6 and 5.2% of births were LBW among non-Hispanic white and

Hispanic women, respectively.[3] Foreign-born black women, however, have lower rates of adverse birth outcomes than U.S.-born black women.[4] Between-population differences in birth outcomes also do not always appear to correspond directly to infant health. Compared to white infants of the same gestational age, black infants born before 37 weeks gestation have lower mortality rates, while black infants completing at least 37 weeks of gestation have higher mortality rates.[1,21]

Rates of adverse birth outcomes also demonstrate temporal differences within and between populations. The rate of preterm birth in the U.S., for example, climbed by more than one-third from the early 1980s to 2006 (although it has dropped in the last two years) and the rate of low birth weight increased by 24% during the same time period.[22] A recent study found that mean birth weight at all term gestational ages has been trending downwards since 1990, after nearly a century of steady increase.[7] Changes in rates of LBW, however, differed between populations defined by race/ethnicity. Between 1990 and 2006, rates increased by 30% for non-Hispanic whites and by 15% for Hispanics, but decreased slightly during the 1990s and rose only 7% from 2000 to 2006 among non-Hispanic blacks.[3]

The traditional epidemiologic focus on individual-level factors associated with birth weight outcomes has not succeeded in explaining these complex between- and within-population variations in rates and distributions of birth outcomes. Individual socioeconomic status, smoking, alcohol and drug use, and utilization of prenatal care have not been found to explain the striking differences in rates of preterm delivery between blacks and whites in the U.S.[1] Further, the downward trend in birth weight from 1990-2005 remains after controlling for length of gestation, singleton status, and maternal race/ethnicity, education, prenatal care, smoking, pregnancy complications, and BMI.[7]

These consistent and unexplained differences between birth outcomes within populations and over time suggest that the determinants of gestational health may include factors beyond the individual level. As described by Rose in his seminal work, the determinants of health measures such as rates and means at the population level cannot necessarily be identified by examining the causes of disease for individuals.[23]

Conceptual framework based on ecologic and evolutionary theory

In this section, I describe a conceptual framework based on principles from ecology and evolutionary theory that may help inform research seeking to understand the determinants of birth outcomes at the population-level in contemporary U.S. settings. Researchers concerned with various health outcomes have discussed the importance of using conceptual frameworks drawn from ecological[24-26] and, more rarely, evolutionary[27,28] principles. Most research examining birth outcomes, especially that which focuses on contemporary U.S. populations, has not used these principles as a basis for hypothesis generation. Evolutionary theory often surfaces in the form of post-hoc explanations for observed epidemiologic associations. However, as stated by Maziak in his 2008 article "The triumph of the null hypothesis", an evolutionary perspective should serve to "formulate hypotheses that are tethered to a framework accepted by most scientists."[29]

Ecological principles. Ecology is the study of the relations between living organisms and the non-living aspects of their environment ("abiotic elements", e.g., sunlight, water, soil composition), and an ecosystem is the environment within which these living organisms and non-living components interact.[30,31] Principles of ecology describe the distribution of organisms, the movement of materials and energy through the system, the succession of ecosystems, and the adaptation of living organisms to their environments.[30,31]

An important ecological principle states that the behavioral and biological characteristics of the living elements in an ecosystem depend in large part on characteristics of the non-living elements and that the relationship between these two sets of elements is homeostatic, i.e. in a stable, constant condition.[32] When the abiotic elements change slowly or cyclically, living organisms alter their behavior or biology in predictable ways to maintain this homeostasis.[31,32] Examples of such responses include seasonal migration in response to cyclical weather events or the gradual shifting of an organism's habitat in response to climate change. Behavioral or biological characteristics in such ecosystems therefore exhibit gradual change over time, but characteristics observed at any one time point will not appear to differ substantially from those observed at a time in the recent past.

Ecologists call changes that alter the organization of the ecosystem in abrupt or unexpected ways "perturbations."[32] Organisms may respond behaviorally and biologically to these changes in ways that appear quite different from their behavior and biology prior to the perturbation and that may be considered "adverse".

Human ecology and health. The idea that ecological theory, originally developed to understand the interactions between non-human animals and their environments, can be applied to the study of human behavior has been the subject of much debate in the social sciences.[30,31] As stated by Catalano, ecological principles can "offer testable explanations of why the incidence of health and [behavior] varies over time in geographically defined populations as well as across such populations at any point in time."[31] An ecological perspective may therefore help us better understand the unexplained between- and within-population differences in birth outcomes.

One of the earliest uses of the phrase "human ecology" occurred in 1914 at a meeting of the British Ecological Society, where human ecology was defined as an "extension of the fundamental principles of ecology into human affairs".[30,33] Sociologists began discussing this concept in the 1920s, when Park, Burgess, and McKenzie described cities and economic bases as ecosystems and used these theories to examine the effects of urbanization on behavior in Chicago.[34] Since this time, scholars have advocated for an ecological perspective on human health in psychology[24] and epidemiology.[25,26]

A human ecosystem includes humans among the living organisms and, among the non-living components, factors such as the economy, social institutions, culture, demographics, and the natural environment. Bronfenbrenner and others have described multiple, nested, and interconnected levels of a human ecosystem and have envisioned the ecosystem as affecting various aspects of human health and development.[24-26] Figure 1 depicts one such ecological model of gestational health that includes levels of influence from the macro (e.g., global, national, regional) to the micro (e.g., local, family, work) to the individual (e.g., behavior, physiology). Factors such as policy, economics, culture, and the natural environment affect the ecosystem at multiple levels.

Application of ecological principles to the human ecosystem suggests that, when aspects of the ecosystem remain constant or change slowly or in an expected pattern, human behavior and biology—and the health sequelae of behavior and biology—will also either remain constant or change slowly or predictably. For example, seasonal weather variation produces predictable changes in rates of infectious diseases (e.g., influenza, malaria, and Lyme disease) and gradual improvements in nutrition have resulted in gradual increases in achieved height in developed nations. When ecological *perturbations* occur, however, humans may exhibit behavioral and biological responses and health sequelae that are unexpected and appear "adverse".[31] Substantial evidence demonstrates associations between ecological perturbations such as economic decline and terrorist attacks and increased incidence of "adverse" health outcomes, such as depression and anxiety, suicide, violent behavior, and substance abuse.[35-37]

Little research has examined the associations between macro-level ecological perturbations, e.g. unexpected economic, political, or environmental change, and birth outcomes (see Chapter II for a review). A related body of literature has demonstrated associations between *micro-level* ecological perturbations, i.e. family- or work-related stressful life events, and low birth weight and preterm birth.[38,39] Research has also documented associations between *static* macro-level factors (e.g., social structure, neighborhood characteristics) and birth outcomes.[2,20] The ecological framework suggests, however, that macro-level perturbations may be as important a determinant of birth outcomes as micro-level perturbations or static macro-level factors. If birth outcomes do in fact respond to ecological perturbations, these changes could help explain some of the temporal variation in birth outcomes in the U.S.

<u>Adaptive responses to ecological perturbations.</u>

As described above, behavioral and biological responses to ecological perturbation likely appear "adverse" because they differ from the behavior and biology of organisms observed before the perturbation. In some cases, however, these responses may represent adaptations to the new ecological circumstance.[31,32] Adaptations have been defined as adjustments to behavior, physiology, or structure that enable organisms to become more suited to an environment .[40] An organism may, for example, adapt to an ecological perturbation such as a drought by migrating to an area that it has not previously inhabited (behavioral) or by going into a dormant state (biological). Adaptive responses are most accurately described as a continuum of responses from fully cognitive (the organism is aware of the response) to fully autonomic (the organism is not aware of the response) and from mostly behavioral to mostly biological (i.e., physiological). The majority of responses have both cognitive and autonomic, behavioral and biological characteristics.

<u>Adaptive responses in human reproduction.</u> Behavioral or biological responses to ecological perturbations that are adaptive also likely increase lifetime fitness of organisms. Lifetime fitness measures the ability of an organism to pass on its genes; an individual human's fitness is reflected in her number of children and her children's own fitness, i.e. number of descendants. Organisms with higher lifetime fitness more likely pass on their genes, implying that, to the extent that adaptive responses are genetically encoded, these responses will be "conserved" by natural selection.

Gestation represents an aspect of human life likely to exhibit evidence of conserved adaptive responses because of its importance in determining lifetime fitness. Behavioral or biological responses to ecological perturbations that improved maternal or offspring lifetime fitness over evolutionary history were likely conserved, such that we may see evidence of these responses following contemporary ecological perturbations.

Two aspects of human reproduction that may represent evidence of conserved responses to ecological change have been described, primarily in the anthropological literature. These two responses, targeted timing of reproduction and plasticity during gestation, may enable mothers to either conserve their own resources for future reproduction or improve their offsprings' chances of survival and future reproduction in the environments faced after birth. The mechanisms through which these strategies operate may be either behavioral or physiological, cognitive or autonomic, or somewhere along the continuum of these responses.[41]

Targeted timing of reproduction. Theory suggests that when environmental circumstances threaten reproduction or survival, women may select against or delay reproduction. Such targeted timing would enable women to conserve their resources and reproduce at a later time when the environment is more favorable for both themselves and their offspring.[42] Amenorrhea (temporary cessation of ovulation) may represent an example of such a mechanism. Amenorrhea occurs in response to temporarily decreased nutrition or increased physical activity, and normal menstruation resumes when nutrition increases or physical activity decreases.[43] Evolutionarily, this may have allowed women to delay conception during times of famine or poor harvest.[42] Ovarian function in contemporary humans has also been shown to respond to changes in maternal health and psychosocial stress, possibly representing evidence of the conservation of this response in modern populations.[44]

Evidence also suggests that women may select against reproduction during times of ecologic stress. A recent study examined associations between state unemployment rates in the year of conception and birth outcomes and maternal characteristics using U.S. data from 1975 to 1999.[45] The authors hypothesized that, if increasing unemployment leads some women to select against reproduction, maternal characteristics and birth outcomes will change with increases in the unemployment rate. The study found that increases in unemployment were associated with increased maternal educational levels, lower rates of smoking and drinking, and lower rates of LBW and very LBW among black mothers only. The authors suggest that these differences result from black women with lower education and worse health selecting against reproduction during economic downturns.

Evidence also indicates that rates of fetal loss, another potential form of selection against reproduction, may increase in response to ecologic perturbations.[44,46] While this form of selection is more costly in terms of maternal investment than selection prior to conception, more information about the fitness of the offspring is available, allowing mechanisms of fetal loss to act selectively based on this information. Evidence from animal literature suggests, for example, that selection in response to ecological conditions depends on both the fitness and sex of offspring. In suboptimal environments, less-fit males are thought to require more maternal investment, yet yield fewer grandchildren, compared to less-fit females.[47] Natural selection, therefore, may have conserved a mechanism that enables selection against male offspring in response to ecologic stress.[47] Research in humans has in fact demonstrated increased male fetal loss during economic downturns[48] and reduced secondary sex ratios (ratios of males to females at birth) following perturbations such as natural disasters[49,50], terrorist attacks[51], economic collapse[52], and community loss.[53]

Plasticity during gestation. Natural selection may also have conserved mechanisms that allow maternal or fetal aspects of gestation to change in response to ecological circumstances. Such plasticity during gestation may a) increase the fitness of the current infant relative to the environment it is likely to encounter at birth[54] or b) reduce the resource burden on the mother to conserve her resources for later reproduction—while still allowing her to produce an offspring from the current gestation.[46] Such responses may occur either later in pregnancy when opportunities have passed for selection by delayed conception or fetal loss, as a less extreme adaptation than fetal loss[55], or when women are older and have fewer remaining opportunities for reproduction.[46]

Examples of potential plasticity. Little research on human reproduction has explored plasticity as a response to ecological perturbation. Potential forms of such adaptive plasticity include alteration to fetal growth rate and achieved size. Reduced or slowed rate of fetal growth when resources are scarce requires fewer maternal resources and may trigger developmental processes that improve survival if the environment remains poor at birth or later in life.[28] The theory of fetal programming (known to many as the "Barker hypothesis") describes such plasticity of growth as well as of metabolic function. Based on Barker's seminal observations that low birth weight is associated with later life disease, this hypothesis states that offspring exposed to inadequate maternal nutrition during gestation adapt by reducing growth and becoming more metabolically efficient.[6,54] A mismatch between a nutrient-poor intrauterine and a nutrient-rich extrauterine environment is thought to result in organisms that are unnecessarily metabolically efficient, resulting in obesity, diabetes, and other poor health outcomes later in life. Many have cited this hypothesis as an explanation for increased rates of obesity and diabetes as countries transition away from subsistence economies, but little research has explicitly tested this hypothesis in humans.[6]

Another possible, though rarely discussed, form of plasticity is accelerated fetal brain and lung maturation in response to stress. A recent review describes evidence of such accelerated development in epidemiologic studies of spontaneous preterm deliveries as well as in experimental animal studies.[56] The authors suggest that this adaptation is obscured in modern contexts by medical interventions increasing the number of non-spontaneous preterm births and saving preterm infants that would not otherwise survive. Although preterm infants today are often smaller and exhibit less mature brain and lung function, the authors state that, prior to recent medical advances (as recently as the 1960s and 1970s), preterm infants that survived showed a low incidence of respiratory distress.[56]

Some have also speculated that the timing of delivery represents an example of adaptive plasticity.[44,46,57] Ellison suggests that the optimal timing of birth is determined by the ability of the mother to meet the nutritional needs of the fetus.[57] When she is no longer able to do this, the fetus may become stressed, signaling parturition. Peacock suggests that in the later weeks of gestation, when fetal brain development requires large maternal nutritional inputs, switching to nutrition via lactation requires less energy than continuing gestation.[46] Little empirical work exists on this topic, however, leaving it a speculative hypothesis.

Potential mechanisms of plasticity. Adaptive plasticity during gestation requires that mothers be able to assess the quality of their current environment for reproduction and the survival of offspring. Mothers must then embody this information, via either behavioral or physiological responses, in a way that affects gestational processes such as fetal growth.

Behavioral or physiological responses to the environment that altered gestation in a way that increased maternal or infant lifetime fitness would have been conserved over evolutionary history by natural selection. Such responses may, as previously described, be either cognitive (conscious) or, more likely, autonomic (subconscious).

The maternal physiological stress response may represent one such reaction to ecological perturbations that affects gestational health. Research demonstrates that a stronger stress response occurs when a stressor is novel, or unexpected, as in an ecological perturbation. Physiological responses to stress are primarily mediated by two systems: the sympathetic-adrenomedullary (SAM) response, a short-term response that includes increased heart rate, stroke volume, and release of energy stores. Activation of the hypothalamic-pituitary-adrenal (HPA) axis is a more prolonged response that is thought to have more long-term effects on health. When the brain perceives a stressor, corticotrophin releasing hormone (CRH) is released from the hypothalamus, stimulating the release of adrenocorticotropic hormone (ACTH) from the pituitary gland, and ultimately the synthesis and secretion of glucocorticoids (GCs) from the adrenal glands.

Animal research has demonstrated that exposure to GCs during gestation reduces fetal growth,[58] and higher levels of CRH are correlated with earlier parturition.[59] Studies in humans examining associations between stress hormones such as GCs and CRH and both maternal self-reported stress and birth outcomes, however, have reported inconsistent associations with both preterm birth[60,61] and low birth weight.[62] These inconsistent findings may reflect the complexity of HPA axis function during human pregnancy. Stress hormones in pregnancy are produced by the mother, fetus, and placenta, with complex feedback and buffering systems regulating transfer of hormones between entities.[63] Attempts to use hormones measured in maternal serum as indicators of "stress" during pregnancy may therefore inadequately represent the experience of the whole system.

Several other physiological adaptations to environments with scarce nutrition have also been suggested.[46] Maternal basal metabolic rates (BMR) appear to respond to maternal nutrition, suggesting that women may be able to alter their metabolism to conserve energy for fetal development.[46] Maternal insulin sensitivity may also decline in order to increase availability of glucose for fetal growth or changes to placenta size, transport efficiency, or blood flow may reduce fetal growth.[46]

Researchers have also proposed epigenetic changes as an adaptation of the genetic structure to the environment during gestation.[64] Epigenetic markers include methyl groups and histone complexes that surround DNA, regulating its structure and accessibility. Factors such as intrauterine nutrition may alter these structures, leading to changes in DNA transcription and protein formation, i.e. altered phenotypic expression.

Maternal behavior change may also represent a mechanism by which women embody information about their environment and affect gestational processes. Women may alter behaviors because of changes in resources such as income, savings, access to medical care, or social support. Self-reported psychosocial stress during pregnancy has been associated with behaviors known to impact birth outcomes including continued smoking after conception[65], poorer nutrition[66], and lower maternal weight gain[67], all of which may affect the physiology of gestation and subsequent birth outcomes.

Application of ecological-evolutionary framework for research on birth outcomes in contemporary settings

The ecological-evolutionary framework described above provides an alternative to examining only individual-level risk factors for birth outcomes and provides a theoretical framework for research that aims to understand the population-level determinants of birth outcomes. However, several important limitations to this perspective should be noted. First, all responses to ecological perturbations may not necessarily be adaptive. Responses that were adaptive in evolutionary history may not remain adaptive today. The Barker hypothesis, for example, suggests that increased metabolic efficiency as a response to restricted nutrition *in utero* leads to increased risk of later-life metabolic and heart disease in settings with abundant nutrition. Humans today may also face ecological perturbations for which there exist no correlates in evolutionary history; responses to such perturbations may or may not be adaptive. Contemporary humans may also exhibit novel responses that were not available during evolutionary history. Maternal smoking or moderate alcohol consumption in response to stress, for example, may reduce fetal growth without improving fitness. Such novel responses may be non-adaptive but—with the help of modern medicine—no longer be subject to natural selection.

Another challenge to utilizing the evolutionary perspective lies in the difficulty of assessing whether an observed change was, in fact, adaptive. It is impossible to ascertain, for example, whether a given mother *would have* had lower lifetime fitness had she reproduced during a drought rather than experiencing fetal loss, or whether an infant with reduced fetal growth *would have* experienced lower lifetime fitness had it been born larger.

Nevertheless, the ecological-evolutionary framework described here may help inform research into the determinants of birth outcomes at the population level in contemporary settings. First, the ecological perspective provides theory to guide exploration of multi-level determinants of birth outcomes. This perspective suggests that perturbations to macro-level aspects of the human ecology may be as important as micro-level or static measures in affecting birth outcomes. Second, the evolutionary perspective helps inform the choice of birth outcome that might respond to such ecologic perturbations. In the next section, I use the ecological-evolutionary framework to generate the primary research question of this dissertation, which examines whether exposure to perturbations to the labor market during gestation is associated with subsequent fetal growth.

<u>Fetal growth as a response to ecological perturbation.</u>

Previous literature has documented evidence that mothers may respond to ecological perturbations by altering the timing of reproduction[42,45,48,51,53,55,68], but less research has explicitly examined mechanisms of plasticity during gestation in response to ecological perturbations. As described above, fetal growth, rate of fetal brain and lung maturation, and timing of delivery may all represent potential sources of plasticity during gestation. Birth weight and gestational age (which can be used to measure both fetal growth and timing of delivery) are most widely available at the population level. Rate of fetal brain and lung maturation are substantially more difficult to measure and not widely available in non-clinical samples. I propose that the evolutionary theory and potential mechanisms of plasticity described above provide more support for the hypothesis that fetal growth (rather than length of gestation) would respond to ecological perturbations than timing of delivery.

First, many of the potential mechanisms of plasticity—i.e., physiological stress response leading to exposure to GCs, alterations to BMR and insulin sensitivity, epigenetic changes, and maternal behavior responses such as altered diet or smoking—are associated with reduced fetal growth. Second, reductions in fetal growth could plausibly increase the lifetime fitness of both mother and offspring. That is, reduced nutrient demands on the mother could conserve resources for future pregnancies, and smaller size could help offspring survive in resource-poor environments after birth. Many have proposed that shortened gestation and preterm birth are associated with maternal psychosocial and physiological stress, suggesting that these might also represent plausible responses to ecological perturbation.[69-71] However, it is difficult to imagine that shortened gestation represents an *adaptive* response. Even "late" preterm births (34-36 weeks) have substantially increased risk of mortality and morbidity. Meanwhile, term infants with birth weights ranging between approximately 2900 and 4100 g are considered healthy[8], suggesting that room for variation in fetal growth may exist. While it remains possible that timing of delivery could respond to ecological perturbation, more theory and consideration of the appropriate measure of this variable are required before it should be pursued as an outcome, and I therefore focus on fetal growth as an outcome in this dissertation.

It is important to note that very small infants would have been unviable throughout most of evolutionary history. Thus, although higher fractions of very small infants—with lower fitness—would result from reduced fetal growth as a response to ecological perturbation, these infants would likely not have survived beyond the first months of life. The surviving portion of a cohort with a down-shifted distribution of weight might more likely survive the tenuous first year of life in a suboptimal environment (due, for example, to lower caloric demands) and have subsequently higher lifetime fitness than a cohort with a higher distribution of weight. (No research has examined this hypothesis, however, and it remains possible that smaller infants have *higher* caloric demands due to compensatory growth.)

I therefore hypothesize that gestations exposed to ecological perturbations in contemporary settings will exhibit reduced fetal growth, as measured by mean birth weight for gestational age. With the advent of medical interventions that save many small infants, I expect to see both decreases in mean birth weight for gestational age and increases in rates of SGA infants in gestations exposed to ecological perturbations.

I also hypothesize that gestations exposed to perturbations in the first trimester will exhibit greater reductions in fetal growth than those exposed in the second or third trimester. Early gestational physiological processes such as implantation, trophoblast invasion, and placental development can affect placental transfer of nutrients to the fetus, subsequently affecting fetal growth.[72-74] Research also suggests that the maternal psychological or physiological stress response remains active in early pregnancy but becomes blunted in the second and third trimester.[69]

The economy as an ecological perturbation.

An important source of ecological perturbation explored by early human ecologists was the economy.[75] These scholars believed that economic principles determined land use, population size, demographic composition, division of labor, and spatial distribution within human communities[31,75] and that these factors were analogous to the spatial and trophic organization in non-human ecosystems. Communities with expanding, contracting, or shifting economic bases would therefore exhibit higher rates of unexpected behavior and biology compared to more stable communities.[31] I therefore investigate perturbations to the economy as a potential determinant of fetal growth at the population level. I specifically investigate the security of the labor market as a measure of ecologic stability vs. perturbation.

A labor market is an arena in which workers compete for jobs and employers compete for workers and is based on the supply and demand of people in a given area who are able and willing to work. The unemployment rate, which equals the number of people seeking work divided by the sum of employed persons and those seeking work, reflects this interplay between supply and demand. More secure labor markets, i.e., those with lower unemployment rates, are characterized by higher supply of jobs and therefore more choice and flexibility for job seekers as well as those currently employed. Higher unemployment rates are associated with higher demand for jobs, less choice for job seekers, and increased anxiety about job security among the employed.[76]

Labor market insecurity may negatively affect the health of those who lose jobs or those who are already unemployed and seeking work. Secure employment provides not only income and benefits, but social support, status, and structure to individuals' lives.[77] Job loss is associated with increased incidence of depression, anxiety, and alcohol consumption. [36,77-79] Those who remain employed in insecure labor markets may also experience stress due to fear of job loss or changed responsibilities at work. Research has shown, for example, that workers surviving a corporate downsizing work harder and experience more fear of layoff than prior to the downsizing.[80] Employed persons who fear job loss far outnumber those who actually lose their jobs.[81] Labor market insecurity also affects families or households in which someone loses a job. Rook and colleagues[82] found that spouses of workers with adverse job events experienced increased depression and demoralization. Family members of job losers may also suffer loss of financial resources or psychosocial stress due to changing roles, time structure, self-esteem, and social support at work or at home.

These sequelae of labor market insecurity may have important impacts on health. Loss of resources, stress and depression, or altered time structure or self-esteem may lead to decreased attention to personal health or to negative coping behaviors, such as smoking or substance abuse. Research has documented increased substance abuse during economic downturns as well as increased incidence of health outcomes such as cardiovascular disease.[36]

Other research, however, has demonstrated associations between labor market insecurity and lower mortality rates.[83-85] Some of this research suggests that more secure labor markets (measured by increases in the employment rate) correspond to decreases in leisure time as individuals work more hours, resulting in less time spent on salutary activities such as physical activity or preventative medical care.[83,86] Increased hours at work may also mean more time spent in hazardous conditions, more job-related stress, and more physical exertion.[83] Other work reports that externalities of labor market insecurity, such as decreased automobile traffic, air pollution, and changes in health care, and not individual behaviors or stress, account for these positive effects on overall mortality rates. [87] Finally, it remains plausible that these positive and negative effects of labor market insecurity on health occur simultaneously, potentially cancelling each other out or leading to different effects in different segments of the population.

Labor market security is a fundamentally macro-level factor characterizing the human ecology. Perturbations to labor market security can affect all individuals living in the labor market area, whether or not they are individually affected by job loss. The security of the labor market can impact communities by affecting funding for public or social services, decreasing philanthropy, impacting environmental quality or changing community networks and depleting social support and capital.[88] The unemployment rate is also commonly reported by the media, and stress or anxiety related to rising unemployment may be experienced by anyone in the labor market area.

Perturbations to labor market security may therefore affect pregnant women regardless of their own or family's employment or financial situation. Women may alter behaviors such as diet, physical activity, consumption of alcohol, tobacco, or drugs, or utilization of health care in response to real or anticipate income or job loss or due to general anxiety about the economy. Psychosocial stress about labor market security may also lead to a physiological stress response.

Research question and hypotheses

In this dissertation, I will examine associations between exposure to perturbations to labor market security during gestation and fetal growth, as measured by birth weight for gestational age. I define perturbations as periods when the labor market is either more secure or more insecure than expected, with the expected value based on the history of the labor market in that area. This definition relates to the ecological principle that organisms respond to abrupt, unexpected changes, i.e. perturbations. Laboratory experiments have also shown that animals exhibit stronger behavioral and biological responses to unexpected, compared to expected, stressors.

I hypothesize that exposure to unexpectedly high labor market insecurity will be associated with reduced fetal growth. High labor market insecurity during gestation may elicit similar adaptive responses to those that humans would have experienced when faced with suboptimal environments (e.g., drought) in evolutionary history, resulting in reduced fetal growth. High labor market insecurity may also lead to changes in maternal behavior and physiology (e.g. changes in diet, smoking, utilization of medical care, activation of the HPA axis or changes in BMR), that are not adaptive and do not represent conserved responses but still result in reduced fetal growth.

On the other hand, I hypothesize that unexpectedly secure labor markets do not correspond to suboptimal environments in evolutionary history and will therefore not lead to reduced fetal growth. Although intuition may suggest that exposure to labor market security will be associated with increased fetal growth, I do not hypothesize that this will happen for several reasons. First, no research of which I am aware—in either contemporary or "primitive" human settings or animal studies—has demonstrated evidence of increased fetal growth following ecologic perturbations during gestation. Second, lower than expected unemployment is less likely than higher than expected unemployment to elicit a response in the population because a) it is less likely to be reported in the media and b) people are less likely to experience stress or anxiety due to lower unemployment. Finally, although some research has demonstrated associations between increasing employment and improved health behaviors and outcomes [83,86], these associations have not been demonstrated in relation to pregnancy behaviors or birth outcomes.

The hypothesized association between labor market perturbations and fetal growth may arise from many pathways. First, pregnant women may personally experience changes in income or employment, *or* they may experience anxiety or stress due to labor market perturbations not accompanied by personal economic change. Either of these pathways may lead to behavioral responses such as changes in tobacco use, diet, or utilization of prenatal care *or* to physiological responses such as activation of stress pathways or changes in metabolism. I will explore whether several of these pathways mediate any observed association between labor market perturbations and fetal growth. Because of the many potential pathways, some of which remain unmeasurable (e.g., anxiety and stress about the labor market, physiological stress, and changes in metabolism), I hypothesize that measurable mediators will explain some, but not all of any observed association.

As previously noted, distinguishing between adaptive and non-adaptive responses to ecological perturbations is difficult, and this research will not attempt to do so. Exposure to labor market perturbations during gestation may lead to reductions in fetal growth that do not confer an advantage in lifetime fitness. Reductions in fetal growth due to worsened maternal health behavior, e.g. smoking, may provide evidence of such non-adaptive responses.

A relatively unexplored hypothesis is that certain populations may differ in their vulnerability to or likelihood of responding to ecological perturbations. Characteristics of populations such as social cohesion and social capital have been shown to affect a variety of health outcomes[89,90] and may serve as buffers against perturbations in some populations. Characteristics of individuals in populations, such as race/ethnicity, socioeconomic status (e.g., wealth, education, and income), coping mechanisms, or self-esteem may also determine how those populations respond to ecological perturbations.[91-94] Previous studies have shown, for example, that the effects of economic contraction on individual financial events and subsequent health outcomes are stronger among middle SES individuals than among low or high SES individuals.[95] Research has also demonstrated associations between economic change and birth rates and sudden infant death syndrome (SIDS) among black, but not white, women.[92,93] I will therefore also examine whether associations between labor market perturbations and fetal growth differ based on maternal characteristics such as race/ethnicity, education, income, or childhood SES. I hypothesize that women with fewer resources—i.e., women of black or Hispanic race/ethnicity, lower childhood SES or educational attainment and women who are unmarried, unemployed, or living in poverty—will be more vulnerable to perturbations to the labor market. These groups will therefore demonstrate stronger associations between labor market perturbations and fetal growth.

Conclusions

Epidemiologic research has made important strides in identifying many individual-level risk factors for adverse birth outcomes such as low birth weight and preterm birth, which carry high clinical, social, and economic costs. Despite this accumulated knowledge, however, we remain unable to explain the differences in the distribution of birth outcomes between populations and within populations across space and time. Although clinicians should continue to focus on improving pregnancy outcomes for individual women and families, epidemiologists and others concerned with understanding the distribution and determinants of birth outcomes at the population level should consider how principles from other population sciences such as ecology and evolutionary theory may inform research on birth outcomes.

Chapter II: Literature review

In this dissertation, I will examine the associations between exposure to an ecological perturbation, i.e. unexpectedly high labor market insecurity and security, during gestation and fetal growth, as measured by birth weight for gestational age. To my knowledge, no prior research has explicitly examined this question. In this chapter, I first briefly review literature on non-economic ecological perturbations and birth outcomes to explore the hypothesis (described in Chapter I) that birth outcomes respond to such perturbations. I then discuss several methodological considerations relevant to research on the association between the economy and birth outcomes. I describe issues related to measurement of the exposure and outcome, study design (aggregate-, multi-, and individual-level), and threats to internal validity. Next, I review studies that examine the association between macro-level economic change and birth outcomes. Finally, I review studies examining the effect on birth weight of individual- and household-level economic perturbations such as job loss and financial problems during pregnancy, which may shed light on one pathway by which macro-level economic change could affect pregnant women.

Macro-level ecological shocks and birth outcomes

In Chapter I, I discuss the hypothesis that birth outcomes may respond to perturbations, acute, unexpected changes, in ecological factors such as the social, political, or natural environment. Here I briefly review several studies investigating a variety of such perturbations and birth outcomes.[69,91,96-107] These perturbations include earthquakes, weather, and the September 11, 2001 terrorist attacks. Overall, findings indicate that birth outcomes appear to respond to ecological perturbations, but findings from these studies are mixed and differ by birth outcome, type of ecological perturbation, population, time period, and methodology.

A study from Haifa, Israel compared obstetric outcome rates from delivery room data in the two weeks before and two weeks following several earthquakes of magnitude 4.0 or greater and reported significantly higher delivery rates in the 48 hours following the events and significantly higher incidence of preterm birth following two of the five earthquakes.[100] Glynn and colleagues assessed stress appraisal and length of gestation in 40 women exposed to the 6.8 magnitude Northridge, California earthquake in 1994.[69] Rating of stress due to the earthquake was higher when women were exposed in either the first trimester of pregnancy or post-partum, compared to exposure in the second and third trimesters. Length of gestation was also shortest among women experiencing the earthquake in the first trimester of pregnancy.

A small number of studies have examined the associations between extreme weather and birth outcomes.[91,99,108] One large time-series analysis covering 13 years in London, United Kingdom found no association between preterm birth and changes in temperature, rainfall, sunshine, relative humidity, and barometric pressure.[99] Another recent study in California found that the increases in weekly ambient temperature were associated with increased rates of preterm birth and that these associations were stronger among younger mothers, blacks, and Asians.[91]

Several studies have attempted to determine whether birth outcomes were affected by the September 11, 2001 terrorist attacks on the World Trade Center (WTC) in New York City. A recent review of this evidence describes five studies examining these associations in the New York City (NYC) area and five studies examining the effects of the event on births in other areas.[101] The latter five studies test the effect of psychosocial stress related to this perturbation on birth outcomes, absent any effect due to direct exposure to, for example, air pollution and particulate matter.

In general, results from these studies are mixed and differ by measurement of birth outcome, control group, and geographic area. Eskenazi and colleagues report an increased odds of births <1500 g and births 1500-1999 g in NYC in the week following the attacks (compared to the three weeks before the attack) but no significant change in the odds of births 2000-2499 g.[96] Berkowitz reported a significant increase in SGA and a non-significant increase in LBW in women acutely exposed to the attacks (close to the WTC on September 11, 2001) compared to a comparison group of NYC women.[102] Lederman and colleagues found lower birth weight and a non-significant increase in risk of SGA in hospitals close to the WTC.[98] In a study not included in the review, Landrigan and colleagues found that women acutely exposed to the attacks had similar risks of LBW to a comparison group of NYC women.[97] Neither Eskenazi and colleagues, Berkowitz, nor Landrigan found a statistically significant difference in preterm birth among women in New York.

Several studies examined birth outcomes among populations not directly exposed to the WTC attacks but suspected to have experienced psychosocial stress due to the event; these groups included births to women delivering in Boston, Massachusetts after (compared to before) September 11[106], births of Arabic name or ancestry living in California and Michigan[103,105], births to active duty military families[104], and births in the Netherlands[107]. These studies report an increased risk of LBW and preterm birth among Arabic births in California but not in Michigan, no significant change in preterm delivery among births to military families, and a reduction in birth weight in the Netherlands.

Overall, studies examining associations between ecological perturbations and birth outcomes have reported overall mixed findings. The two studies of earthquakes and preterm birth provide some evidence that very stressful ecologic perturbations may be associated with preterm birth. The studies examining the September 11, 2001 terrorist attacks appear to demonstrate modestly decreased birth weight and increased risk of LBW and/or SGA, but find no effect on preterm birth. Findings from the studies described above differ, however, by population, time period, and methodology. In some cases, authors compared similar populations at different points in time (e.g. before and after an earthquake or September 11)[69,91,96,99,100] and in others, authors compared a presumably exposed population to a presumably unexposed population[96-98,102]. In the case of research on the WTC attacks, it is not known whether any population, especially in the U.S., was truly "unexposed" to this dramatic event. Further, some studies attempt to explicitly deal with potential seasonal variation in both exposure and birth outcome[91,96,99], while others do not. Finally, much of the previous research examines birth weight and LBW outcomes, which conflate effects of ecological perturbations on length of gestation and fetal growth.

Overall, this body of literature does provide some evidence that ecological perturbations are associated with changes in birth outcomes. Further research is needed to better understand what types of ecological perturbations matter most, which aspects of the gestational process are actually affected (length of gestation or fetal growth), and which populations or subgroups are most vulnerable or respond most strongly. In the following section, I review literature examining economic change—the broad category of ecologic perturbation that I pursue in my dissertation research—and birth outcomes.

Review of literature on economic change at the ecologic and individual level and birth outcomes

Methodological considerations for research on the association between economic change and birth outcomes. Before reviewing the literature on economic change and birth outcomes, I first discuss several important methodological considerations for this type of research. In the following review of the literature, I discuss the extent to which these methodological concerns potentially affect the validity of findings from the reviewed studies. At the close of this section, I describe how my research will attempt to improve methodologically on previous research.

Measurement of economic variables. In my study, I propose to use the unemployment rate because it estimates the security of the labor market for employees and job seekers, as described in Chapter I. Although most other research examining the association between the economy and birth outcomes has also used the unemployment rate, available indicators of U.S. economic strength for the U.S. (from the Bureau of Labor Statistics) also include the employment to population ratio, wages, and measures such as consumer spending and gross domestic product. All of these measures represent different aspects of the underlying construct of the strength of the economy. Few studies have examined the comparative utility of these variables for predicting changes in health.[109]

The unemployment rate equals the number of people seeking work divided by the sum of employed persons and those seeking work. Despite this variable's widespread reporting and intuitive appeal as an economic indicator, a limitation is that increases in the unemployment rate often occur in the same month that the number of employed persons increases because the number of persons looking for work tends to increase when the economy expands. Insecure labor markets can also discourage persons from seeking work, causing the unemployment rate to drop even when the total number of employed persons decreases. Research, however, does suggest that the unemployment rate is associated with increased incidence of health outcomes such as depression, anxiety, suicide, and alcohol consumption.[36,77] Moreover, the unemployment rate remains the measure most widely reported by the media, and may therefore act as a stressor even on those who do not personally experience unemployment.

Differing treatments of economic indicator variables in the literature also complicate interpretation and comparison of findings across studies. Most studies use continuous measures, which imply linear effects of increasing and decreasing unemployment across its distribution. Others have examined measures of economic change *per se*, i.e. the difference between a current value of unemployment and the previous value, while others have used investigator-defined recessions (binary variables).

The unemployment rate and other economic indicators exhibit substantial autocorrelation over time, i.e. secular trends, cycles, and the tendency for a time series to remain elevated or depressed, or to oscillate, after high or low values. Comparisons of crude unemployment rates may therefore provide limited information about the health of the economy. The unemployment rate in June, for example, may be consistently higher than the rate in May (due to recent graduates entering the labor market); comparing these two values without taking this seasonal autocorrelation into account would provide the false inference that the economy had worsened from May to June.

Methods for dealing with autocorrelation include seasonal adjustments and first-differencing (subtracting the rate in the current month from the previous month rate to remove secular trends). These techniques, however, may not adequately address other types of autocorrelation such as cycles or oscillations. The most flexible decomposition methods are those developed by Box and Jenkins and known as ARIMA models (described in detail in Chapter III).[110,111] These models use rule-based strategies for estimating the value of any datum from the best-fitting model of autocorrelation in the history of the data to that point. This process "decomposes" the original data into expected values (based on autocorrelation) and residual values (observed values minus expected values). The residual values express the degree to which the variable differs from its expected value based on its own history. Residual values of zero indicate no difference in the observed and expected values while non-zero values represent deviations from the expected value, or "unexpected" values.

Other challenges in defining the economic variable of interest include specifying the most appropriate unit of analysis (e.g., nation, state, metropolitan area) and lag time (i.e., how long economic shocks take to affect human mood, behavior, or health).[109] One study attempted to compare the ability of economic measures to predict mood and frequency of stressful life events.[109] Findings indicated that economic conditions one to three months prior affected the dependent variables and that regional measures predicted better than metropolitan area measures (although a combination of regional and metropolitan measures predicted better than either alone). In terms of availability, ease of calculation, and robustness of correlation with behavioral indicators, unemployment was reported as the best predictor. Economic change *per se* was more strongly associated with life events (which could represent both desirable and undesirable events) while undesirable economic change (i.e., economic contraction) was more strongly associated with mood.

Study design. Studies examining the associations between an ecologic variable, such as an economic measure, and birth outcomes fall into two categories of design: aggregate (or "ecologic studies") and multilevel. Studies examining the association between individual job loss or income loss and birth outcomes are purely "individual-level" studies. Aggregate studies compare rates of birth outcomes during time periods or within populations characterized by exposure to the macro-level variable (e.g., high vs. low unemployment). Studies may also compare multiple populations at multiple time periods. Multilevel designs, on the other hand, compare birth outcomes of individual gestations characterized by exposure to the macro-level variable (e.g., high vs. low unemployment). This can be done using large datasets, such as vital statistics records, or smaller survey or clinical samples. The advantage of these designs is that information is available on the joint distribution of potential individual-level confounders and the exposure and outcome.[112] That is, data on characteristics of individual gestations such as maternal age, race, and SES, are available and can be controlled in the analysis (discussed in more detail below). To the extent that data are available, multilevel designs can also explore potential differences in associations by individual characteristics or mediation by variables such as maternal behaviors.

Threats to the internal validity in ecologic studies. Threats to internal validity in aggregate-level studies have received less attention in the literature than threats to the internal validity of individual- or multilevel studies and therefore deserve brief discussion. As in individual-level studies, a primary threat to internal validity stems from third variables that are associated with the exposure variable and cause the outcome variable, i.e., confounders.

Data used in aggregate-level studies often come from archival sources (e.g., the US Bureau of Labor Statistics, birth certificates), rather than original data collection, and these secondary sources rarely include measurement of potential confounding variables such as maternal characteristics or behaviors. The aggregate-level study design allows for control of such variables only by including the proportion of the population with a characteristic (e.g., race or level of education) in the model. The unknown joint distribution of potential confounders with exposure and/or outcome can lead to substantial confounding bias.[112]

Catalano and colleagues suggest several strategies for defending against confounders omitted from a test either because the author did not suspect or could not measure them.[113] First, omitted confounders that would presumably affect the outcome of interest in other populations as well as the test population (i.e., "generally-occurring" confounders) can be addressed by including a measure of the outcome in a comparison population as a covariate in a regression model of the outcome in the study population. A comparison population is defined as one exposed to the suspected confounder but not to the same exposure of interest as the test population. An example of such a generally-occurring confounder in a study of economic change and birth outcomes would be a general trend toward more medical interventions at birth, which might affect birth outcomes and also be associated with general economic growth in multiple populations (e.g., U.S. states). Another method for addressing such generally-occurring confounding is to include a measure of general trend (e.g., year) or an indicator variable (i.e., a fixed effect) for each time period (e.g., months, years), thereby controlling for generally-occurring changes in the outcome over time.

Although comparison methods can correct for generally-occurring confounders, they cannot reduce the threat of confounders peculiar to the test population or when the dependent variable has not been measured in a comparison population. An example of a confounder peculiar to the test population might be increased migration to one U.S. state; such a change in the demographics of the population might be associated with economic change in that state and result in changes in birth outcomes. When the omitted variable in such circumstances presumably exhibits autocorrelation in time, a strategy called decomposition can be used. Decomposition involves removing autocorrelation from either the independent or dependent variable (or both) such that shared autocorrelation can no longer confound the association. For example, if the unemployment rate is hypothesized to affect birth weight, and both exhibit seasonality and secular trends, removing these two forms of autocorrelation from both variables will prevent confounding by those variables. Variables exhibiting secular trends may be decomposed by adjusting for a population-specific slope over time. More rigorous ARIMA decomposition can remove all types of autocorrelation from the dependent variable, the independent variable, or the relationship between the two.

Only replication of findings in multiple populations can reduce the threat of omitted third variables that exhibit no autocorrelation and affect only the test population. Such a variable would be equivalent to a one-time phenomenon that occurred only in the test population, e.g. a natural disaster. If an association survives decomposition and comparison as well as control for suspected and measured covariates, finding it again in other populations implies that the association did not arise from an omitted confounder unique to the original test population. Although one published article can include a finding and its replication[114], replications occur more frequently in subsequent research studies.

Threats to internal validity in individual- and multilevel studies. Three threats to validity, or categories of bias, for individual- and multilevel studies have been thoroughly discussed in the epidemiologic[115] and social sciences[116] literature; these include confounding, information, and selection bias. In literature examining individual economic contraction (e.g. job loss or financial problems) and birth outcomes, confounding by maternal or family characteristics presents an important threat. Women who experience economic difficulties during pregnancy may differ from those who do not on important characteristics that also predict birth outcomes; higher self-reported health, for example, is associated with employment and higher income status as well as with better birth outcomes. In multilevel studies that examine macro-level economic contraction (e.g. rising unemployment or recession) and individual birth outcomes, women's likelihood of living in an area where such events occur may depend on maternal health, socioeconomic, or demographic characteristics that also affect birth outcomes. Confounders such as those described in the previous section can also lead to bias when the exposure is a macro-level economic variable. Similar strategies, such as controlling for a measure of the birth outcome in a comparison population, decomposing variables thought to exhibit autocorrelation, or using time or place fixed effects can reduce bias due to omitted confounders in multilevel studies.

Measurement of birth outcomes also represents a potential source of information bias. Accurate and consistent measurement of "gestational age" at birth has challenged researchers for decades and remains a topic of controversy.[117,118] Length of gestation can be quickly and cheaply estimated for almost all pregnancies by simply calculating the amount of time between birth and the mother's last menstrual period (LMP). Although this remains the most commonly used measure, LMP can be subject to substantial error due to problems with recall and inconsistency of women's menstrual cycles. Other methods such as ultrasound or clinical assessment based on maturity at birth may provide more accurate measures. Biased estimates of association may arise in studies using length of gestation if the method of or accuracy of measurement differs between groups characterized by exposure (e.g. those exposed vs. not exposed to economic contraction) or other important maternal characteristics. Self-reporting of variables presents an additional concern in that many maternal characteristics, i.e. education, income, age, race/ethnicity, may also affect *how* women report on economic situation or birth outcomes, leading to an additional source of measurement bias.

Selection bias occurs when both exposure and outcome variables are associated with inclusion of data in analysis.[115] A critically important manifestation of selection bias in this literature may include gestations that do not end in a live birth. If, as suggested in Chapter I, less-fit (i.e., smaller or less healthy) gestations more often end in spontaneous abortion or fetal loss during stressful times, live births from cohorts exposed to macro-level stress may actually be larger and/or more healthy. Maternal selection into conception may also represent a source of bias if the data cannot accurately distinguish between women exposed to a stressor during gestation and those exposed prior to gestation. Women choosing to conceive during stressful times may differ from those who do not in ways that affect observed birth outcomes.[45]

<u>Ecologic economic change and birth weight outcomes.</u> A small number of studies have examined the associations between economic change or contraction and birth weight outcomes.

In an early multilevel study, Fisher and colleagues found that the proportion of LBW births increased during the recession of 1982 (compared to 1980) in Washington State within low-income (crude relative risk [RR] = 1.18, 95% CI = 1.00, 1.25) but not high-income census tracts (crude RR = 0.98, 95% CI = 0.77, 1.25).[119] This finding suggests that the association between economic contraction and birth weight may depend on factors such as personal or community resources. The authors did not find evidence of confounding using analyses stratified by maternal age, race, marital status, parity, time since last birth, and previous fetal or infant loss, although they did not explore multivariable confounding by these factors.

Two other early multilevel studies by Joyce[120] and Joyce and Mocan[121] investigated the association between the unemployment rate and rates of LBW among blacks and whites in New York City and in Tennessee in the 1970s and 1980s, respectively. These studies did not address other individual-level variables besides race. The New York study examined de-trended unemployment rates but did not address other types of autocorrelation. The Tennessee study decomposed the unemployment rate into two components: cyclical (due to the business cycle) and structural (the inherent ability of the economy to provide jobs for those who seek them). Both studies report null associations. This early work is notable in that the authors identified several key analytical issues, such as trends and cycles in unemployment, upon which later work builds.

Catalano and Serxner[122] examined the effect on birth weight of a natural experiment, in which state workers in Sacramento County, California were unexpectedly told to prepare for pay cuts and lay-offs in June, 1978. The decision to reduce state workers was reversed, however, and none actually lost their jobs. The threatened lay-offs were associated with increased LBW among white and Hispanic infants exposed to the threat in the fourth and third month of gestation, respectively. The authors estimated the risk of LBW attributable to the threatened lay-offs as approximately 2.6% in white male infants and 7.4% in Hispanic male infants. This finding suggests that stress—due to the threatened layoffs—may have affected gestational health in the absence of any actual job loss.

In the same paper, these authors examined the effect of unexpectedly low total monthly employment (derived using ARIMA methods) in the Los Angeles (LA)-Long Beach metropolitan areas of California on odds of LBW. Lower than expected employment was associated with increased incidence of LBW among male infants of white and Hispanic ethnicity.

This study used ARIMA modeling to identify and remove seasonality and other forms of autocorrelation and included the total number of live births as a control variable in both tests to account for potential changes in fertility rates. The authors did not use comparison or replication methods to further address potential confounding by omitted third variables, nor did they address any individual characteristics of gestations other than race. The authors acknowledge that, although the event in Sacramento County was extreme in nature, other communities that rely heavily on one or a few employers may have similar experiences when these employers threaten to reduce jobs. The LA County analysis may be more generalizable to large, diverse metropolitan areas.

In a separate study, Catalano and colleagues also report a significant positive association between quarterly increases in numbers of unemployed males and rates of very LBW (<1500 g) in analyses of data from Norway and Sweden between 1973 and 1995.[123] The authors estimated that approximately 2.1% of all very low weight births were attributable to increased male unemployment in this period. The authors used ARIMA decomposition methods to control for autocorrelation and comparison and replication methods to reduce potential confounding by unmeasured third variables. This study is notable in that it may provide evidence that economic contraction can indirectly affect pregnant women when unemployment increases among males.

Bremberg examined rates of low birth weight in the Stockholm, Sweden area in periods before, after, and during a recession from 1991 to 1996.[124] In this aggregate-level analysis, there was no significant difference in the mean rate of low birth weight in the recession period (44.0 per 1,000) compared to the mean rate in the previous and following periods combined (44.4 per 1,000). Bremberg did not adjust for any other potentially available covariates, nor did he address potential confounding by omitted third variables. This inadequate control for confounding leaves open the possibility that an association is being masked by an omitted third variable.

In a recent study, Schempf and Decker examined the association between the state unemployment rate and preterm LBW births among black women in the U.S. from 1990 to 2002.[94] The authors included state and month indicator variables to address potential confounding by state of residence and seasonality. They report that a one percent increase in the unemployment rate was associated with a two percent increase in odds of preterm LBW birth (OR = 1.02, 95% CI: 1.01-1.03). This association remained after adjusting for maternal age, parity, prenatal care, and smoking. The stated purpose of this study was to determine whether the decreasing unemployment rate during this time period "explained" the decreasing rates of preterm LBW among black women during this period. Schempf and Decker therefore included indicator variables for each year from 1990-2002 and assessed the overall significance of that set of variables before and after controlling for monthly state unemployment. The trend of decreasing black preterm LBW was not explained by state unemployment but was explained by maternal characteristics. These findings could alternatively be interpreted to mean that the monthly state unemployment rate was associated with black preterm LBW, even after controlling for national economic changes using these year indicator variables. A weakness of this study is that a 1% change in the monthly state unemployment rate may reflect autocorrelation in this variable and not represent a meaningful measure of the economy from month to month; this study would be strengthened by using ARIMA methods to remove autocorrelation from the unemployment rate.

These studies examining the associations between measures of macro-level economic contraction and birth weight outcomes demonstrate overall mixed findings. The two studies that use the most rigorous methods to measure the economy and to defend against confounding by omitted third variables[122,123] suggest that rates of LBW and/or very LBW may increase following economic perturbations. As previously discussed, however, using birth weight alone as an outcome conflates effects on both length of gestation and fetal growth. Making inference from these findings about the effect of economic perturbation on the process of gestation is therefore not straightforward.

Individual-level economic change and birth outcomes. Using data on births between 1981and 1994 from the National Longitudinal Survey of Youth (NLSY79), Dooley and Prause tested the association between individual-level birth weight and mother's change from adequate employment (defined as employment that is not poverty wage or involuntary part-time) to either unemployment, involuntary part-time employment, or poverty wage employment during pregnancy.[125] The authors report that women who moved from adequate employment to unemployment or involuntary part-time employment during pregnancy delivered significantly lower weight (β(SE) = -185.43 (77.2) and -418.05 (165.2) grams, respectively) infants compared to women who remained adequately employed. The odds of LBW were also significantly higher (odds ratio [OR]: 7.38, 95% confidence interval [95% CI]: 1.82, 29.89) for women moving to involuntary part-time employment.

The NLSY79 is a nationally representative sample of individuals who were 14 to 22 years old at enrollment in 1979. These data allow specification of many potential confounders including maternal pre-pregnancy weight, alcohol use and smoking during pregnancy, weight gain during pregnancy, and length of gestation. Other unexamined potential confounders include maternal life-management skills, general health, pregnancy complications, and own birth weight [17]. Although the NLSY79 had very high retention rates,[126] selection bias could also have affected the results of the analyses. Inclusion in the study was dependent on follow-up after pregnancy, which may be related to both adverse employment changes during pregnancy and infant birth weight. The self-reported nature of employment and birth weight data could have lead to differential measurement error by factors such as maternal education, leading to bias in the reported association.

Interpretation of findings from this study depends on interpretation of the variable defined as "shift to inadequate employment". Some women may have chosen to switch to low wage jobs during pregnancy to avoid the greater physical and psychological demands of higher-paying jobs. Depending on a woman's financial and family circumstances, these shifts may or may not result in significant loss of resources or greater stress. Inclusion in this study also depended on adequate employment prior to pregnancy, and their findings may only generalize to women who begin pregnancy employed.

This study is of particular relevance to the empirical research presented in this dissertation because I also utilize the NLSY79 dataset. My study population will, however, include births up to the year 2000 and will not exclude women without adequate employment prior to pregnancy. Issues from this study that may also affect my research are the lack of data on mother's own birth weight and pregnancy complications, the self-reported nature of the data and potential for measurement error, and selection bias due to loss to follow-up.

A small number of other studies have also demonstrated higher risks of low weight and preterm births among women experiencing adverse job or financial events during pregnancy. Binsacca reports that women with LBW infants had a relative risk of reporting financial problems during pregnancy of 5.9 (95% CI: 3.3, 10.5), compared to women with a >2500g birth.[38] The author defined financial problems as any mention in the woman's medical record of self-reported financial hardship during pregnancy, including inability to pay rent or buy food, unemployment of self or partner, and loss of medical insurance. Hedegaard reports that births ending preterm had 2.3 (95% CI: 1.1, 4.8) times higher probability of self-reported "substantial income drop" during pregnancy than births ending at term.[39] Although both studies suggest that personal economic change may be related to gestational health, these findings should be interpreted with caution as the self-reported nature of the data may induce bias if unmeasured characteristics of women are associated with likelihood of reporting such an event and also with birth outcomes.

This research examining individual-level economic events during pregnancy may shed light on one pathway by which ecologic economic change could affect birth outcomes. These individual-level events, however, do not necessarily occur during ecologic economic perturbations, and should not be thought of as proxy measures for the macro-level economy.

Methodological and conceptual contributions of my dissertation research to previous literature

The literature reviewed in this chapter suggests that ecological perturbations such as earthquakes and terrorist attacks may affect birth outcomes, although much is still unknown about what type of perturbation matters, what aspects of gestation are affected and how, and what populations are most vulnerable. In my dissertation research, I will examine associations between a specific ecological perturbation, i.e. unexpected changes in labor market security, and birth weight for gestational age. Previous research examining associations between economic change and birth outcomes has demonstrated mixed findings. In the most rigorous studies, macro-level economic change appears to lead to increased rates of LBW and very LBW. Findings from the Dooley and Prause and other individual-level studies also suggest an association between individual-level economic change and decreased birth weight and increased risk of low birth weight, suggesting one pathway by which macro-level economic contraction may affect birth weight.

My dissertation research will contribute to the existing research both conceptually and methodologically. I will utilize a multilevel design, combining macro-level data on unemployment rates with individual-level data on birth outcomes, characteristics of gestations such as maternal race/ethnicity, age, education, employment, income, and behaviors during pregnancy. Individual-level data will come from the National Longitudinal Survey of Youth 1979 (NLSY79), an ongoing prospective cohort study that enrolled men and women 14 to 22 years of age in 1979.[127] The NLSY79 has gathered data on education, employment, income, pregnancy, and birth outcomes from 1979 until the present.

The multilevel design will allow me to control for individual characteristics of gestations known to be associated with birth weight outcomes that may also be associated with exposure to labor market perturbation, reducing potential confounding bias by these variables, whereas previous research on the macro-level economy and birth outcomes has generally considered few individual-level variables beyond race/ethnicity.

Births to women in the NLSY79 take place between 1982 and 2000 and in all 50 states. This temporal and geographic variation will allow me to employ strategies to defend against potential confounding by omitted third variables. First, I will be able to control for any temporal trends or time period-specific patterns shared by both labor market perturbations and fetal growth (comparison). Second, the multiple states in this study serve as a replication tool to ensure against confounding by place-specific factors.

Several previous studies have provided evidence that the association between ecological perturbations and birth outcomes does differ by race/ethnicity or SES.[91,94,122] The multilevel design of my study will allow me to explore whether any discovered associations between labor market perturbations and fetal growth differ by characteristics such as maternal race/ethnicity, educational attainment, and income. The longitudinal nature of this data will also allow me to examine whether these associations differ by childhood SES.

Little research has explicitly examined the mechanisms through which the macro-level economy could affect birth outcomes. The research demonstrating associations between individual financial or employment change and birth outcomes suggests that this may represent one pathway. Fisher hypothesizes that the recession decreased access to prenatal care for low-income women; Catalano and colleagues suggest that maternal psychosocial stress increases risk for preterm delivery, leading to increased rates of low and very low birth weight; and Joyce and colleagues suggest that changes in utilization of prenatal care, consumption of tobacco, alcohol, and drugs, and maternal weight gain affect birth weight. The multilevel design of my research will allow me to investigate whether individual financial change and/or maternal pregnancy behaviors mediate any discovered associations between exposure to labor market perturbation and fetal growth.

Unlike previous studies that have focused on either LBW or preterm birth, my study will use birth weight for gestational age to measure fetal growth. As discussed in Chapter I, fetal growth is a biologically plausible response to changes in maternal behavior and physiological stress. Theoretically, fetal growth may represent a plausible adaptive response to ecological perturbations conserved through evolutionary history. Birth weight for gestational age also explicitly measures only fetal growth without conflating possible effects of labor market perturbations on fetal growth and length of gestation.

A further contribution of my study will be the theoretically and methodologically motivated measurement of labor market perturbations. As described in this chapter, the unemployment rate at the state level is more strongly associated with depression and stressful life events than other state-level economic indicators and indicators at the metropolitan area level[109], and is more frequently reported by the media than local measures. I will therefore use the state-level unemployment rate in the mother's state of residence during pregnancy to describe the labor market security during that gestation. I will also use the monthly (instead of annual) unemployment rate, allowing me to characterize labor market security during each trimester of gestation.

I will use rigorous ARIMA modeling methods to remove autocorrelation from the unemployment rate and to then identify periods in which the unemployment rate was statistically significantly above or below its expected value based on the ARIMA models. This methodology addresses the issue of autocorrelation in the unemployment rate—which makes raw values difficult to compare to each other—and also removes any potential autocorrelation that could be associated with fetal growth, reducing potential confounding by omitted third variables. Much of the previous research on the associations between the macro-level economy and birth outcomes has used either continuous measures of the unemployment rate (e.g., changes in unemployment or deviations from expected values) or perturbations defined by the author (e.g., recessions). The methodology that I will employ represents a rigorous and objective way of classifying labor market perturbations as periods of unexpectedly high or low state unemployment, taking into account autocorrelation in the past history of unemployment in that state.

Research questions and hypotheses

Aim 1: Examine the association between exposure to state-level labor market perturbations (i.e., unexpectedly high insecurity and security) during each trimester of gestation and fetal growth, as measured by birth weight for gestational age percentiles.

a) Hypothesis 1: Exposure to unexpectedly high labor market insecurity during gestation will be associated with lower mean birth weight for gestational age percentile and higher risk of being born small for gestational age (SGA).

b) Hypothesis 2: Exposure to unexpectedly high labor market insecurity in the first trimester will be more strongly associated with reduced birth weight for gestational age percentile and SGA, compared to exposure in the second or third trimester.

c) Hypothesis 3: Exposure to unexpectedly high labor market security during gestation will *not* be associated with birth weight for gestational age percentile or SGA.

Aim 2: Examine whether any observed association between exposure to labor market perturbations during gestation and birth weight for gestational age percentile differs by maternal characteristics (race/ethnicity, childhood socioeconomic status, educational attainment, marital status, employment status, or poverty status).

a) Hypothesis 1: The association between exposure to labor market perturbations during gestation and birth weight for gestational age percentile will be stronger among women of non-white race/ethnicity, low childhood SES, low educational attainment, and those who are unmarried, unemployed, or living in poverty,.

Aim 3: Investigate whether the association between labor market perturbations during gestation and birth weight for gestational age percentile is mediated by individual economic change (i.e., changes in maternal employment status or household income) or maternal pregnancy behaviors (i.e., smoking, first trimester utilization of prenatal care, or gestational weight gain). If associations are mediated by one or more of these factors, calculate the proportion of the total association explained by these pathways.

a) Hypothesis 1: Some, but not all of the association between labor market perturbations during gestation and birth weight for gestational age percentile will be mediated by individual economic change.

b) Hypothesis 2: Some, but not all of the association between labor market perturbations during gestation and birth weight for gestational age percentile will be mediated by maternal behaviors.

Chapter III: Methods

Study population and data

Study population. The study population for this analysis included gestations and births to women ages 15-44 enrolled in the National Longitudinal Survey of Youth 1979 (NLSY79). The NLSY79 is an ongoing prospective cohort study started in 1979 that was designed to capture information on the educational attainment, labor market experiences, family transitions, and fertility of a nationally-representative sample of 6,283 females and 6,403 males. Participants were between the ages of 14-22 at enrollment. The majority of the data in the NLSY79 are collected during in-person interviews with respondents; some interviews are conducted by telephone for logistical reasons.

This dataset is well-suited to my study questions for several reasons. First, individual-level data on state of residence, birth date, and length of gestation allow me to geographically and chronologically link state-level economic data to specific gestations, enabling identification of gestations as either "exposed" or "unexposed" to labor market perturbations during each trimester. Further, the national and longitudinal nature of the NLSY79 ensures substantial variability in labor market conditions across gestations in the dataset. Third, the NLSY79 contains substantial information on women's behaviors during pregnancy as well as socioeconomic status (including income and education), employment, and marital status for a period of approximately 25 years. Such variables may represent important confounders, effect measure modifiers, or mediators of the association between labor market perturbations and fetal growth.

Sampling and survey procedures. The NLSY79 is based on an original random sample of U.S. housing units combined with a random sample of Department of Defense records. The initial sample was used to identify persons between the ages of 14 and 21 on December 31, 1978 who were then asked to participate in the NLSY79. All who completed the first interview are considered members of the cohort and were placed in one of three stratified samples:

1) "a cross-sectional sample (6,111) designed to represent the noninstitutionalized civilian segment of young people living in the United States in 1979 and born January 1, 1957, through December 31, 1964"
2) "a set of supplemental samples (5,295) designed to oversample civilian Hispanic or Latino, black, and economically disadvantaged, nonblack/non-Hispanic youths born in the same time period"
3) "a military sample (1,280) designed to represent the population born January 1, 1957, through December 31, 1961, serving in the military as of September 30, 1978."

Births to women in NLSY79 are not nationally representative, but do represent a diverse, national sample of births to women who were between the ages of 14 to 22 in 1979. More information on sampling in the NLSY79 can be obtained from the User's Guide.[126]

The majority of data from the NLSY79 are publically available online (https://www.nlsinfo.org/investigator/pages/login.jsp). To ensure respondent confidentiality, these public-use data files do not include geographic variables (e.g. state of residence) or personal identifiers (e.g., date of birth). I obtained this data, available in a protected "Geocode Data" file, through a licensing system established by the Bureau of Labor Statistics (BLS) (http://www.bls.gov/nls/nlsfaq2.htm#anch31). The **Committee for Protection of Human Subjects at the University of California, Berkeley waived the requirement for formal review of this research.**

Structure of data. Participants in NLSY79 were surveyed annually from 1979 to 1994 and biannually since 1994 to the present (latest data available at time of analysis are from 2006 wave). All surveys cover a variety of topics including family structure, educational attainment, income, work history, and a limited set of health variables (e.g., height, weight, and health limitations that prevented the respondent from working in the past year).

Study sample. NLSY79 began collecting data on pregnancies and birth outcomes in 1983 and includes data for 8,397 births to 4,233 women in all 50 states, Washington DC, and Puerto Rico. I excluded multiple births (n=115) and births with missing data on maternal state of residence during pregnancy (n=223), birth weight, or gestational age (n= 1302 [331 missing only birth weight, 300 missing only gestational age, 671 missing both]). I also excluded 42 births with either gestational ages < 20 weeks (n=2), gestational ages >44 weeks (n=12), or implausible combinations of birth weight and gestational age using the criteria established by Alexander and colleagues (n=28).[128] The study sample included 6,715 births between the years of 1982 and 2000.

Definition of variables in NLSY79

The Appendix lists and briefly describes the variables used to characterize these births.

Variables assessed during birth interview. The following variables were available from the birth questionnaire given to NLSY79 women in the first survey after a birth: infant sex, maternal age at birth, maternal pre-pregnancy and pre-delivery weight, birth weight, length of gestation in weeks, and birth date.[129] I subtracted the length of gestation from the birth date to obtain an estimated first day of gestation. Women also reported on whether they had smoked in the 12 months before the birth and in what month they first accessed prenatal care. I used this data to create a binary maternal smoking variable and a measure of first trimester (1-3 months) vs. later (≥4 months) utilization of prenatal care.

Maternal demographics, health, and socioeconomic status. NLSY79 defined participants as black, Hispanic, or non-Hispanic/non-black at baseline, and I used this variable to describe maternal race/ethnicity. Of the original NLSY79 participants, those classified as non-Hispanic/non-Black primarily self-identified as being of European descent (68%), with the rest self-identifying as being Asian/Pacific Islander (1%), American Indian (8%), "American" (9%), or other (14%).

I used the longitudinal structure of the data to describe maternal educational attainment, employment status, marital status, poverty status, general health, and state of residence as close as possible to the estimated first day of gestation for each birth. That is, I used the value of the variable from the survey conducted in the year of the birth, if available. If these data were not available (either because the mother did not participate in NLSY79 in that year or because the NLSY79 did not conduct a survey in that year), I substituted values from the prior survey not more than two years before the first day of gestation. For state of residence, I also included values up to two years after the birth if data from before the birth were missing.

Maternal body mass index and gestational weight gain. I used the value of maternal pre-pregnancy weight taken from the birth questionnaire, if available. Otherwise, I used the procedure described above for demographics to obtain a pre-pregnancy weight as close as possible to the beginning of each gestation. Height was only reported in the first six years of the survey, as participants are assumed to have reached their full height after 1985. For births before 1985, I used the maternal height reported closest to the birth, and for births after 1985, I used the 1985 height.

I calculated maternal body mass index (BMI) as kg/m^2. I considered a BMI of <15 or >50 implausible and set its value to missing (n=4 and n=16, respectively). I calculated maternal gestational weight gain as the difference between the pre-delivery weight in kg reported on the birth questionnaire and the estimated pre-pregnancy weight in kg. Because a part of maternal gestational weight gain is the weight of the infant, I subtracted the birth weight of the infant to obtain net gestational weight gain.

Maternal childhood socioeconomic status (SES). Prior research has shown that childhood SES as measured by parental education is associated with adult health in a dose-response relationship, i.e. lowest levels of education are associated with worst health outcomes.[130] At the baseline survey in 1979, participants reported their parents' level of education. I categorized women as having low childhood SES if their father had <12 years education, average childhood SES if their father had 12 years of education, and high childhood SES if their father had >12 years education.

Individual economic change variables. Participants were asked about their employment history since the last survey including each job held, whether they had left any job, the last date of work at that job, and the reason for leaving that job. Women who reported leaving a job on a date that fell between their estimated first day of gestation and the birth date of the child were classified as having job loss during pregnancy if the reported reason for leaving was: "layoff," "fired," "plant closed," "program ended," or "end of temporary or seasonal job". Women reporting quitting for pregnancy, family, or other reasons were not classified as having job loss during pregnancy.

I also used the longitudinal structure of the data to calculate whether households of mothers shifted from non-poverty status to poverty status ("household entered poverty") or reported lower income ("household income loss") in the survey closest to the birth compared to the previous survey.

<u>Birth weight for gestational age outcomes.</u> Much research examining economic indicators and birth outcomes uses low birth weight as the primary outcome. Birth weight, however, reflects both fetal growth and length of gestation, while birth weight for gestational age represents a more precise measure of fetal growth that takes into account length of gestation. Because small changes in fetal growth could have important implications for later life health, I examined changes in both mean birth weight for gestational age and the rate of "small for gestational age" infants.

I used criteria developed by Alexander and colleagues[128] to remove implausible combinations of birth weight (g) and gestational age and then calculated birth weight for gestational age percentiles (hereafter called "birth weight percentiles") using previously published tables that compare infants to a U.S. sample from 1999-2000.[8] I used the standard definition of small for gestational age (SGA) to classify infants below the 10th percentile of weight for age as SGA.

Perturbations to labor market security during pregnancy

I examined perturbations to monthly labor market security during gestation as the independent variable, i.e. exposure, in these analyses. Using monthly (as opposed to annual) measures allowed me to specify the exposure status of trimesters of individual gestations in the NLSY79 dataset. I measured monthly labor market security using state unemployment rates from 1976-2000 for all 50 states, Washington DC, and Puerto Rico. These data are publically available from the Bureau of Labor Statistics (BLS).[131] The unemployment rate equals the number of people seeking work divided by the sum of employed persons and those seeking work, and measures the security of the labor market for job seekers, job holders, families, and communities (as described in Chapter I).

Previous research suggests that increases in the unemployment rate at the state level are more strongly associated with depression and stressful life events than a) other state level economic indicators and b) indicators at the metropolitan area level.[109] The state unemployment rate is also more frequently reported by the media than local measures and can be estimated with more precision than the unemployment rate in metropolitan areas due to larger sample sizes.

I defined perturbations to labor market security as follows: Months in which the state unemployment rate was higher than its statistically expected value were classified as having unexpectedly high labor market insecurity (one type of perturbation). Months in which the state unemployment rate was lower than its statistically expected value were classified as having unexpectedly high security (another type of perturbation). Perturbations, as described in Chapter I, represent abrupt or unexpected changes to the ecosystem. This definition identifies months in which the unemployment rate was significantly different than that which would have been expected based on its history.

Calculating the statistically expected value of the unemployment rate requires taking into account time-dependent correlation between values. This "autocorrelation" includes secular trends, cycles, and the tendency to remain depressed or elevated following high or low values. If data are trending, for example, values will be correlated with and predicted by the value at the preceding time point. If data exhibit cycles, such as seasonality, values will be correlated with and predicted by values from, for example, the same month in the preceding year.

Autocorrelation in time series data implies that the comparisons between the crude values of any two data points in the series are not necessarily meaningful. An increase in the unemployment rate between, for example, December and January, may simply reflect seasonal patterns in which the rate is always higher in January. The expected value of the series is therefore dependent on autocorrelation and does not simply equal the mean of the series. Researchers use several approaches to adjust time series data for autocorrelation, including indicator variables for day of week, month, or year; time-by-place interaction terms to adjust for place-specific autocorrelation; splines, quadratic and cubic functions, etc. Flexible methods for assessing and accounting for autocorrelation in a time series known as ARIMA modeling were developed by Box and Jenkins; these methods model autocorrelation based on the observed data (instead of using pre-specified parameters such as year indicator variables).[110,111] In order to obtain statistically expected values of the unemployment rate time series, I employed ARIMA modeling to identify and model autocorrelation in the monthly unemployment rate in each state from 1976-2008.

ARIMA modeling. Generally, Box-Jenkins methods model autocorrelation using autoregressive, integrative, and moving average (ARIMA) parameters.[111] Integrative parameters include "first differencing" (i.e., subtracting the values of month *t* from those of month *t-1*) to model trending data or differencing at $t=12$ to model seasonality. Autoregressive and moving average parameters model the tendency of a time series to remain elevated or depressed following a perturbation. Autoregressive parameters describe autocorrelation that persists for relatively long periods and may be characteristics of the input variable itself, while moving average parameters describe more transient patterns that may represent external input.

Estimation of ARIMA models results in the following:

$$Z_t = \frac{(1 - \theta B^n)\, a_t}{(1 - \emptyset B^n)}$$

where Z_t represents the expected value of the variable (e.g., the monthly unemployment rate) at time *t* after applying the ARIMA parameters; *a* is the observed value of the time series at time *t*; B is the value of *a* at time *t-n*; θ is the Box-Jenkins moving average parameter, and φ is the Box-Jenkins autoregressive parameter.

Box-Jenkins methods are a set of systematic routines for identifying ARIMA parameters of a time series (i.e., the monthly unemployment rate for each state). Investigators may specify *a priori* which parameters they suspect should be included in the model, either based on visual inspection of the data or outside knowledge about the series (e.g., knowledge that the unemployment rate exhibits seasonality). Investigators may also use routines in ARIMA modeling software that seek the best fit model based on the data alone.

After model estimation, the investigator can assess model fit by examining the autocorrelation function (ACF) and the partial autocorrelation function (PACF). The ACF represents the correlation between values z_t and z_{t-n} , while the PACF represents the correlation between z_t and z_{t-n} controlling for the ACF of z_t and $z_{t-(n+1)}$. If the ACF or PACF indicate remaining autocorrelation, investigators may choose additional ARIMA parameters to include in the model. Various models can be compared for fit.

ARIMA models therefore decompose the observed variable into its statistically expected values based on autocorrelation (z_t). The statistically expected value for each time point is based only on the history of the time series up to that point, not on future values. The residuals from an ARIMA model, which measure the difference between the observed (a_t) and statistically expected (z_t) values, exhibit constant variance, no autocorrelation, and have a mean of 0. These residuals represent deviations from the expected value and thus capture perturbations in the time series.

ARIMA modeling of monthly state unemployment rate. I used software from Scientific Computing Associates (SCA) to perform ARIMA modeling of the monthly state employment rate, estimating a separate ARIMA model for each of the 50 U.S. states, Washington D.C., and Puerto Rico using data from 1978-2000. I first used the "iarima" routine in SCA, which identifies the best fit ARIMA model based on the data. I specified *a priori* that the routine should specifically examine higher order autocorrelation at lag 12 (i.e., *t*-12 months) because the unemployment rate usually exhibits seasonality. I inspected the parameter estimates from the models estimated by iarima to ensure that no parameters in any of the models violated the assumption of stationarity (were not close to or greater than 1.0). I also inspected the ACF and PACF for additional higher order correlation. For six states, I found evidence of violations of stationarity and/or higher order correlation after running iarima. For these six states, I specified an alternative ARIMA model based on my visual inspection of the ACF and PACF and re-estimated the model. I then estimated the correlation between the z_t values from my model and those from the model specified by the iarima routine. All of the correlation coefficients exceeded 0.92, and four of six were higher than 0.97, demonstrating that my alternative models also fit the data well. I therefore used my alternative models for these six states to avoid violations of stationarity.

Next, I used an SCA routine to identify months with statistically significant (t-value ≥ 2.7) differences between a_t, the observed unemployment rate, and z_t, the statistically expected unemployment rate based on the ARIMA model. I classified these months as having unexpectedly high labor market *insecurity* if these residual values (a_t - z_t) were greater than 0 (i.e., the unemployment rate was higher than statistically expected) and as having unexpectedly high labor market *security* if the residuals were less than 0 (i.e., the unemployment rate was lower than statistically expected). These months therefore had unemployment rates either above or below the 99.5% confidence interval, i.e. were extreme outliers. I created two binary variables to classify each month on insecurity (1= unexpectedly high insecurity, 0 = not unexpectedly high insecurity) or security (1= unexpectedly high security, 0=not unexpectedly high security). Many months had a 0 for both variables, indicating that labor market security in that month was not unexpectedly high or low.

Figure 2 demonstrates the total number of labor market perturbations (in all states in the U.S.) identified using the method described above. Figure 2 demonstrates that the recession of the early 1980s was characterized by years with many months of unexpectedly high labor market insecurity at the outset (1980-1982) followed by years with many months of unexpectedly high labor market security (1983-1984). The recent U.S. recession of 2008-2009 is also characterized by years with many months of unexpectedly labor market insecurity. The number of months per year with labor market security or insecurity will not correlate exactly with the national unemployment rate for two reasons. First, labor market security is state-specific. Second, these labor market perturbations are deviations from the expected value at each time point; months with high insecurity or security may therefore occur when the general employment situation of a state or the nation is relatively secure or insecure.

Exposure classification. I merged the monthly residuals of the state unemployment rate and the binary variables for labor market insecurity and security from the ARIMA models described above with the NLSY79 birth data by woman's state of residence during pregnancy. In order to assign these values to months of individual gestations (which do not correspond to calendar months), I assigned each gestation a "conception month." The conception month was the month of the estimated first day of gestation if that estimated day fell before the 15th of the month. If the estimated first day of gestation fell on or after the 15th of the month, then the following month would be the "conception month." This takes into account that the first two weeks of gestation estimated from last menstrual period (LMP, the most common method of assessment during the time period of the study) usually fall prior to conception. This method also takes into account that births conceived at the end of a month would experience less than half of the unemployment experience of that month. I also characterized the last month of gestation as the month in which the infant was born if the birth date was on or after the 15th of the month and as the month before the infant was born if the birth date fell before the 15th of the month. This takes into account that infants born before the 15th of the month are exposed to less than half of the unemployment experience of that month during gestation. I then characterized the first (months 1-3), second (months 4-6), and third (months 7-9) trimester of each pregnancy as exposed to labor market insecurity if any of the months of that trimester were classified as having unexpectedly high insecurity and as exposed to labor market security if any of the months of that trimester were classified as having unexpectedly high security. This procedure created two sets of three independent indicator variables which I will notate as A1, A2, A3 (exposed vs. not exposed to high labor market insecurity during the first, second, and third trimester of gestation, respectively) and B1, B2, B3 (exposed vs. not exposed to high labor market security during the first, second, and third trimester of gestation, respectively) for each individual gestation in the dataset.

Statistical methods.

The sampling strategy of the NLSY79 may lead to bias due to oversampling of Hispanic or Latino, black, economically disadvantaged nonblack/non-Hispanic youths, and military youth. The NLSY79 provides sampling weights, but states that these weights are not appropriate when analyses are not conducted on the entire sample or in regression analyses.[126] NLSY79 recommends adjusting for sampling characteristics; I therefore include indicator variables for each of the oversampled groups in my multivariable analyses. (Univariable and bivariable analyses therefore represent test of parameters with regards to a target population represented by the relative proportions of the sampling strata.) Unless otherwise noted, all analyses were conducted using SAS version 9.1 (SAS Institute, Cary, NC).

Univariable analyses. I first examined the univariable mean and standard deviation (SD) of maternal age and birth weight percentile, the proportion of gestations exposed to labor market insecurity and security in the first, second, and third trimester of gestation, and the proportions of variables describing individual characteristics of gestations (variables listed in Appendix A).

Bivariable analyses. I examined the difference in mean birth weight percentile and proportion of SGA births among gestations exposed vs. unexposed to labor market insecurity and labor market security during each trimester (six separate tests). For birth weight percentiles, I used independent two-sample, two-tailed t-tests, and for SGA, I used Pearson chi-square tests.

I also examined box plots of birth weight percentile by the binary labor market perturbation variables for each trimester to detect variations from normality, skewness, or outliers or differences in the variance of the outcomes within exposure groups.

Key analytical issues. Aim 1 of this analysis seeks to determine whether mean birth weight for gestational age percentile or the odds of SGA differ between gestations exposed vs. unexposed to labor market insecurity or security during each trimester of gestation. Several key analytic issues related to this aim are considered below.

Correlation by state of residence: Birth weight for gestational age percentile outcomes may exhibit within-in state correlation (i.e., non-independence), which may result in incorrect inference (i.e., standard error) derived from statistical models. In this analysis, I use generalized estimating equations (GEE) with exchangeable correlation to account for correlation between births in the same state in the dataset.

Potential confounding by shared temporal trends of dependent and independent variables. The presence of shared temporal trends or patterns between labor market perturbations and birth weight for gestational age outcomes in this data could lead to confounding bias. This would occur only if, for example, both the probability of labor market perturbations occurring during each trimester of pregnancy and the mean birth weight for gestational age of the births in the sample both decreased or increased over the study period or were both high or low at certain points in the study period, due to extraneous forces (e.g., migration, changes in population age distribution, major natural disasters or weather events, etc.) In order to explore this possibility, I examined plots and models of both the labor market perturbation and birth weight for gestational age variables over time in my data.

I first plotted the probability of exposure to labor market insecurity and security in the first, second, and third trimesters of gestation, the mean birth weight for gestational age percentile, and the proportion SGA in the study sample over the study period (1982-2000). I visually inspected these graphs for shared trends or patterns between the exposure and outcome variables. I then used logistic regression models to determine whether the odds of either type of labor market perturbation (insecurity or security), the mean birth weight percentile, or the odds of SGA were predicted by linear trends (using a continuous variable for year of birth). I estimated these models accounting for within-state correlation of outcomes using GEE. If findings from this exploration of trends and patterns over time indicated that any specific labor market perturbation measure shared a trend or pattern with either birth weight for gestational age outcome over the study period in my data, I would then control for such shared temporal patterns in my multivariable analysis.

Potential confounding by individual characteristics of gestation. Characteristics of individual gestations such as maternal race/ethnicity or SES are not expected to confound the association between labor market perturbations and birth weight for gestational age outcomes in this analysis. Although these variables have been shown in the literature to be associated with birth weight outcomes, they should not be associated with the probability of a labor market perturbation occurring in a given state during a woman's pregnancy (i.e., labor market perturbations are exogenous shocks). However, the age of mothers in the sample increased over the study period because of the longitudinal cohort design, suggesting that individual characteristics of births in the early part of the study period (births to younger mothers) may differ from those in the latter part (births to older mothers). If the probability of labor market perturbations occurring during pregnancy also exhibits a temporal trend (as described above), this could lead to potential confounding due to coinciding age and period effects.

I therefore estimated multivariable models adjusted for characteristics of births that may have changed as the NLSY79 sample aged: maternal age as a continuous variable, indicator variables for maternal race/ethnicity, educational attainment (<12 or >12 years), marital status, below federal poverty level, parity, and pre-pregnancy BMI categories (underweight, overweight, and obese), and indicator variables for "missing" data (cite).

Aim 1: Primary analysis. Aim 1 seeks to determine whether mean birth weight for gestational age percentile or odds of SGA differ between gestations exposed vs. unexposed to two types of labor market perturbations (i.e., unexpectedly high insecurity and security) during each trimester of gestation. For this analysis, I estimated four primary multivariable models. I used linear regression models to estimate the association between A1, A2, and A3 (indicator variables for exposed vs. not exposed to labor market insecurity during the first, second, and third trimester of gestation, respectively) and birth weight for gestational age percentiles (Model BW_A). I also used linear regression models to estimate the association between B1, B2, and B3 (indicator variables for exposed vs. not exposed to labor market security during the first, second, and third trimester of gestation, respectively) and birth weight for gestational age percentiles (Model BW_B). I then used logistic regression models to estimate associations between A1, A2, and A3 and SGA (Model SGA_A) and between B1, B2, and B3 and SGA (Model SGA_B). In each model, I included labor market perturbations in all trimesters in the same model to estimate the association between, for example, exposure to labor market insecurity in the first trimester and birth weight percentile, holding labor market insecurity in the second and third trimesters constant.

Models BW_A and BW_B: I used multivariable linear regression models with the following basic form:

$$\mathrm{E}\left(Y_{ij} \middle| \mathrm{A}_{ij}, \mathrm{W}_{ij}\right) = \beta_0 + \beta_1\left(\mathrm{A1}_{ij}\right) + \beta_2\left(\mathrm{A2}_{ij}\right) + \beta_3\left(\mathrm{A3}_{ij}\right) + \beta_{4-k}\left(\mathrm{covariates}_{ij}\right)$$

where i = birth, j = state, Y = mean birth weight percentile, and β_1, β_2, and β_3 = the mean differences in Y comparing gestations exposed vs. unexposed to labor market insecurity in the first (A1), second (A2), and third (A3) trimesters—holding all individual covariates $\beta_{4\text{-}k}$ (listed above) constant. I used the Wald test of the null hypothesis that β_1, β_2, or β_3 are not significantly different from 0 with an alpha of 0.05. I then estimated the same model substituting B1, B2, and B3 for A1, A2, and A3 to examine the mean difference in Y comparing gestations exposed vs. unexposed to labor market security in the first, second, and third trimesters.

Models SGA_A and SGA_B: To examine the binary SGA outcome, I used a multivariable adjusted logistic regression model as follows:

$$\log \frac{P(Y_{ij}|\mathrm{A}_{ij}, \mathrm{W}_{ij})}{1 - P(Y_{ij}|\mathrm{A}_{ij}, \mathrm{W}_{ij})} = \beta_0 + \beta_1\left(\mathrm{A1}_{ij}\right) + \beta_2\left(\mathrm{A2}_{ij}\right) + \beta_3\left(\mathrm{A3}_{ij}\right) + \beta_{4-k}\left(\mathrm{covariates}_{ij}\right)$$

where i = birth, j = state, Y = SGA and $\exp^{\beta 1}$, $\exp^{\beta 2}$, and $\exp^{\beta 3}$ represent the ratio of the odds of SGA comparing gestations exposed vs. unexposed to labor market insecurity in the first (A1), second (A2), and third (A3) trimesters—holding all individual covariates $\beta_{4\text{-}k}$ (listed above) constant. I estimated the same model substituting B1, B2, and B3 for A1, A2, and A3 to examine the ratio of the odds of SGA comparing gestations exposed vs. unexposed to labor market security in the first, second, and third trimesters.

Sensitivity analyses.

State of residence: additional analysis. All models described above used GEE to account for within-state correlation between birth weight percentile outcomes. If certain states have more frequent labor market perturbations, gestations in those states may also have a higher probability of exposure to perturbations. If these states also have higher or lower birth weight for gestational age, this could result in a spurious association. No *a priori* reason suggests that states with either high or low probabilities of labor market perturbations should also differ on birth weight percentile outcomes; however, I compared estimates and standard errors from my original models to (non-GEE) regression models using state indicator variables to control for this potential source of bias.

I also compared estimates from the original models to GEE models accounting for correlations between births to the same mother (both with and without state indicator variables) to ensure that additional within-mother correlation did not exist. If these models yielded similar estimates of the association between exposure to labor market perturbations (i.e., β_1, β_2, and β_3 from above models within 0.5 birth weight percentile points) and standard errors (within 0.1), I planned to continue to use the original GEE model specifying correlation at the state level only.

Shared temporal trends: additional analysis. I used visual inspection of the plots of labor market perturbations and birth weight percentile outcomes over the study period to determine whether to conduct additional analyses to address potential shared temporal trends. If this visual inspection showed possible shared temporal patterns other than linear trends, I planned to conduct sensitivity tests using indicator variables for either year of birth and/or periods of birth. This modeling approach controls for effects of years or periods (e.g., five year periods) during which exposure and outcome variables exhibit shared patterns. Inclusion of these indicator variables increases stratification of the data and therefore reduces precision of estimates. These variables may also make findings more difficult to interpret because, for example, indicator variables for year may effectively "control" for national economic downturns, the effect of which I do not necessarily wish to remove from my estimates. I therefore planned to only include these variables in my main analysis if these sensitivity tests indicated that controlling for them substantially changed estimates of association from primary models.

As an additional check for confounding by time, I fit a model that regressed birth weight percentiles on state-by-year of birth interaction terms to create expected and residual (observed – expected) values for birth weight percentiles adjusting for state-specific linear temporal trends. I then examined the effect of labor market perturbations in each trimester on those residual values (using the same form as Models BW_A and BW_B). If state-specific trends do not explain any association between labor market perturbations and birth weight for percentiles discovered in Aim 1, estimates and standard errors from these models should be similar to those from Models BW_A and BW_B.

Other measures of labor market perturbation. I examined associations between labor market perturbations in the three months prior to each gestation and birth weight percentile outcomes to explore whether labor market perturbations have a lagged effect on birth weight percentile outcomes.

I also examined the association between the continuous residuals of the unemployment rate from the ARIMA models and birth weight percentile outcomes. These residuals equal the difference between the observed unemployment rate in a month and its expected value—based on autocorrelation from its past values—and therefore represent less extreme labor market perturbations than the binary variables used in the primary analysis. I used separate models to examine the positive and negative residual values in each month of gestation as the independent variable to estimate the effects of less extreme labor market insecurity (positive residuals) and security (negative residuals) on birth weight percentile outcomes.

Other individual covariates: Certain maternal health conditions are known predictors of birth weight, e.g. preeclampsia and diabetes. The only measure of maternal general health consistently available in NLSY79 surveys over time asks if the participant had any health conditions limiting her ability to work in the past year. Because this variable is only a rough estimate of maternal health conditions relevant for pregnancy and because it may actually represent a mediator in the relation between exposure to labor market perturbations and birth weight outcomes, I chose not to include this in the primary analysis and instead conducted a sensitivity analysis to determine whether its inclusion affected the estimates of association from models BW_A and BW_B and SGA_A and SGA_B. I also examined models controlling for maternal employment status during pregnancy.

Aim 2: Effect modification. Aim 2 seeks to examine whether associations between exposure to labor market perturbations during gestation and birth weight for gestational age percentile differ by maternal characteristics, specifically, race/ethnicity, childhood SES, educational attainment, employment status, marital status, and poverty status. (Such differences in measure of association will be referred to as effect modification for brevity.)

I decided *a priori* to explore effect modification only for associations between labor market perturbations and birth weight percentile found to be significant in Aim 1. If, for example, labor market insecurity was associated with birth weight for percentile in the first trimester only, I only explored effect measure modification for this trimester. I also examined effect modification for only the continuous outcome variable, birth weight percentile. Rothman[115]and others[132] have discussed that additive models (e.g., linear regression) including interaction terms between an exposure and a third variable provide a more interpretable result than multiplicative models (e.g., logistic regression) and are therefore preferred for this type of analysis.

I assessed potential effect modification by including interaction terms between labor market perturbations variables and each of the potential effect modifiers (maternal race/ethnicity, childhood SES, educational attainment, employment status, marital status, and poverty status) in separate models. I used indicator variables for each of these effect modifiers (described in Appendix A). Some variables took two levels and required only one indicator variable (e.g., poverty status [1 or 0]), while others took more than one level and required multiple indicator variables (e.g., race/ethnicity: black/non-Hispanic [1 or 0] and Hispanic [1 or 0] with white/non-Hispanic as the reference group).

I first examined the distribution of labor market perturbations by trimester stratified by potential effect modifiers to determine whether the sample size was adequate to stratify analyses by these characteristics. I then used two-sample, two-tailed t-tests to compare the mean birth weight for gestational age percentile between women exposed and not exposed to labor market perturbations within categories of potential effect modifiers to examine the unadjusted association between labor market perturbation and birth weight percentile within these categories.

Finally, I implemented regression models with the following general form (using the example that only exposure to labor market insecurity in the first trimester was found to be significantly associated with birth weight percentile in Aim 1):

$$\mathrm{E}(Y_{ij}|\mathrm{A}_{ij}, \mathrm{W}_{ij}) = \beta_0 + \beta_1(\mathrm{A1}_{ij}) + \beta_2(\mathrm{A2}_{ij}) + \beta_3(\mathrm{A3}_{ij}) + \beta_4(Z_{ij}) + \beta_5(\mathrm{A1}_{ij} * Z_{ij}) + \beta_{6-\mathrm{k}}(\mathrm{covariates}_{ij})$$

where i = birth, j = state, Y = birth weight percentile, A1 = exposure to labor market insecurity in the first trimester, A2 and A3 = exposure to labor market insecurity in the second and third trimesters, respectively, and Z = effect modifier indicator variable. (If, for example, labor market insecurity in *both* the first and second trimester showed a significant association in Aim 1, interaction terms of A1 and A2 with the potential effect modifier would be included.) β_1 quantifies the difference in birth weight percentile comparing gestations exposed vs. unexposed to labor market insecurity in the first trimester for women with a 0 value for the effect modifier indicator variable; $\beta_1 + \beta_5$ quantifies the difference in birth weight percentile comparing gestations exposed vs. unexposed to labor market insecurity in the first trimester among women with a 1 value for the effect modifier indicator variable. For effect modifier variables with multiple levels, the model was expanded to include multiple indicator variables and interaction terms.

I examined Wald tests of statistical significance for interaction terms in these models with a conservative p-value cut-off of 0.20. [133] When effect modification was present, I reported the linear combination of β coefficients describing the difference in birth weight percentile associated with labor market perturbations in each subgroup.

Aim 3: Mediation. Aim 3 seeks a) to investigate whether any discovered associations between exposure to labor market perturbations during gestation and birth weight percentile are mediated by individual economic change or maternal pregnancy behaviors and, if so, b) to calculate what proportion of the total effect of labor market perturbations on birth weight percentile is explained by the indirect effect through the mediator variable. I measured individual economic change by examining maternal job loss, household entering poverty, and household income loss in year prior to birth. Maternal pregnancy behaviors included smoking, first trimester utilization of prenatal care, and net gestational weight gain. As with the analysis for Aim 2, I decided *a priori* to pursue Aim 3 only for associations between labor market perturbations and birth weight percentile outcomes found to be significant in Aim 1 and to only examine mediation for the continuous outcome variable, birth weight percentile. I used indicator variables for each of the potential mediators (described in Appendix A) except for net gestational weight gain, which was a continuous variable.

I first examined the distribution of labor market perturbations by trimester stratified by potential mediators to determine whether the sample size was adequate to stratify analyses by these characteristics. I then used two-sample, two-tailed t-tests to compare the mean birth weight for gestational age percentile between women exposed and not exposed to labor market perturbations within categories of potential mediators to examine the unadjusted association between labor market perturbations and birth weight percentile within these categories.

Estimating total, direct, and indirect effects. The analysis conducted for Aim 1 evaluates the total association between exposure to labor market perturbations during gestation and birth weight for gestational age outcomes, i.e., the *total effect* of exposure on outcome regardless of pathway. This analysis seeks to examine whether these total effects are mediated by *indirect effects*—i.e., pathways through which the exposure acts on the outcome—and to calculate what proportion of the total effect is explained by these mediating pathways. The difference between the total effect and indirect effects is often referred to as the *direct effect*. In this analysis, the portion of the total effect not explained by these particular mediators may still explained by other, unmeasured mediators (e.g., maternal stress, other behaviors, etc.). The term *direct effect* may therefore be misleading, but I use it to describe the difference between the total and indirect effects for consistency with previous literature.

Direct effects have been described as either "controlled" or "natural".[134] Controlled direct effects represent the difference in the outcome comparing exposed and unexposed individuals and "setting" the intermediate variable to the same level for both exposed and unexposed. Natural direct effects represent the difference in the outcome comparing exposed and unexposed individuals but allowing the intermediate variable to take the value that it would have been had the person been unexposed. If certain assumptions are met, then the controlled and natural direct effect are equal, and standard additive (i.e., linear) regression models will provide an estimate of both. These assumptions are 1) the exposure and intermediate variables do not interact to affect the outcome and 2) no unmeasured confounding of the exposure and intermediate relationship exists.[134] If the exposure and intermediate variable do interact to affect the outcome, then the controlled and natural direct effects are not equal, and standard linear regression models can provide something like an average of the two estimates.

In this analysis, I included as confounders the continuous year variable and the same individual characteristics of gestations as in Aim 1 (maternal age, race/ethnicity, education, marital status, poverty status, pre-pregnancy BMI, and parity). I assumed no unmeasured confounding of the exposure and intermediate variable. Although it is possible that other maternal characteristics could affect individual economic change or maternal behaviors (e.g., personality characteristics, mental health, wealth, etc.), it is unlikely that these variables would be associated with exposure to labor market perturbations during gestation.

I investigated whether any of the potential mediators of interest interact statistically with exposure to labor market perturbations in models of birth weight percentile using the methods described in Aim 2. I used the Wald test with an alpha of 0.20 to test the null hypotheses that the association between labor market perturbations and birth weight percentile does not differ across levels of the potential mediators (no additive statistical interaction).

If this analysis led me to accept the null hypothesis of no statistical interaction, I planned to then estimate models including each of the proposed mediators as follows (again using the example that only labor market insecurities in the first trimester were found to be significantly associated with birth weight percentile in Aim 1):

Total effect:

$$\mathrm{E}(Y_{ij}|\mathrm{A}_{ij},\mathrm{W}_{ij}) = \beta_0 + \beta_1^{\mathrm{T}}(\mathrm{A1}_{ij}) + \beta_2(\mathrm{A2}_{ij}) + \beta_3(\mathrm{A3}_{ij}) + \beta_{4-k}(\mathrm{covariates}_{ij})$$

Direct effect: $E(Y_{ij}|A_{ij}, W_{ij}) = \beta_0 + \beta_1^D(A1_{ij}) + \beta_2(A2_{ij}) + \beta_3(A3_{ij}) + \beta_4(Z_{ij}) + \beta_{5-k}(\text{covariates}_{ij})$

where i = birth, j = state, Y = birth weight percentile A1 = exposure to labor market insecurity in the first trimester, A2 and A3 = exposure to labor market insecurity in the second and third trimesters, respectively, and Z = the potential mediator. β_1^T represents the total effect of labor market insecurity in the first trimester on birth weight percentile—i.e., the difference in birth weight percentile comparing gestations exposed vs. unexposed to labor market insecurity in the first trimester holding only covariates and labor market insecurity in the other two trimesters constant. β_1^D represents the direct effect of labor market insecurity in the first trimester on birth weight percentile —i.e., the difference in birth weight percentile comparing gestations exposed vs. unexposed to labor market insecurity in the first trimester, controlling both individual covariates and the indirect effect mediated through Z.

I then used β_1^T and β_1^D to calculate the proportion of the total effect of exposure to labor market insecurity that is explained by the mediator, i.e., the proportion explained (PE). The PE equals the total effect minus the direct effect, divided by the total effect ($\frac{[\beta_1^T - \beta_1^D]}{\beta_1^T}$).[135]

If the first step of this analysis demonstrated interaction between the exposure and mediator variables, I planned to then report three separate effects to describe the relationship between labor market insecurity, the mediator variable, and birth weight percentile: the total effect, the direct effect when Z=1, and the direct effect when Z=0 (personal communication, Alan Hubbard, 2011). In this case, I will not calculate a proportion explained.

<u>Treatment of missing data.</u>

Missing data on exposure or outcome. Of the 8,282 singleton births with detailed information on pregnancies and birth outcomes in the NLSY79 dataset, a substantial proportion was missing (or had implausible values for) birth weight and/or gestational age (16.2%), and a smaller proportion was missing maternal state of residence during pregnancy (2.7%). These missing data affect the number of observations with available data on both exposure to labor market perturbations (the calculation of which relied on both state and gestational age) and birth weight for gestational age percentile outcomes (the calculation of which relied on both birth weight and gestational age).

The main analyses described above were complete case analyses, which use only observations with complete data on both exposure and outcome. This method has been shown to be unbiased when data are either missing completely at random (MCAR) or missing at random (MAR).[136,137] Data are MCAR if the outcome Y is unconditionally independent of the missingness of Y, i.e. missingness is generated by a random process. Data are MAR if the outcome Y is conditionally independent of the missingness of Y, given the covariates in the analysis model.[137]

Although assumptions of MAR can never be proven, I examined predictors of missing data on exposure and outcome as follows to determine if the MAR assumption is reasonable for these data. First, I examined logistic regression models predicting missingness of both exposure and outcome using the individual covariables from my analytic models (i.e., maternal age, race/ethnicity, pre-pregnancy BMI categories, educational attainment, poverty status, marital status, parity, and sampling characteristics). Second, I used Pearson chi-square tests to determine whether observations missing the exposure variable (labor market perturbations) differed significantly on the outcome (birth weight for gestational age percentile) from those not missing exposure data and whether observations missing the outcome variable differed significantly on the exposure.

Simple methods for imputing outcome or exposure data (e.g. mean imputation) have been shown to induce more bias than complete case analysis or multiple imputation methods. While multiple imputation methods for outcome or exposure data will increase the efficiency of effect estimates, these methods also rely on the assumption of MAR. If my exploration of missingness (described above) suggests that the MAR assumption is reasonable, I will continue using a complete case analysis.

Missing data on individual covariables. Data were also missing on several key individual characteristics used as covariables in this analysis. Of the 6715 gestations in the main analytic sample, 2.0% were missing maternal education (n=132), 1.9% were missing marital status (n=126), 11% were missing poverty status (n=739), and 12.1% were missing pre-pregnancy BMI (n=810). When data are missing on covariables, multiple imputation analysis may reduce bias. [137] I therefore conducted a sensitivity analysis using multiple imputation to impute values for all missing covariables.

Multiple imputation creates new datasets by replacing each missing value with a value randomly drawn from the range of plausible values. I used PROC MI in SAS 9.1 to create five imputation datasets, which has been shown to be adequate with high efficiency for cases with few missing data (SAS 9.1 PROC MI help file). I then used PROC MIANALYZE to re-analyze models from Aim 1 using these imputed datasets and combining the results to obtain the correct inference (SE). This procedure takes into account the uncertainty inherent in drawing random values for the imputed values when calculating standard errors.

Missing data on potential effect modifier or mediator variables. Several key variables for Aims 2 and 3, i.e. potential effect modifiers or mediators, also had substantial missing observations. Specifically, of the 6715 observations with complete data on the main exposure and outcome, 14.5% were missing data on childhood SES (n=971), 9.7% were missing data on employment status (n=649), 3.2% were missing data on month of prenatal care (n=214), and 12.5% were missing data on net maternal weight gain during pregnancy (n=145). A small percentage (0.2) of gestations were missing data on maternal smoking during pregnancy (n=12), and as described above, 2% were missing educational attainment and 11% poverty status.

For potential effect modifier or mediator variables that were missing >10% of observations (childhood SES, net gestational weight gain, and poverty status), I used the methods described above to explore the predictors of missingness on these variables and whether missingness of these variables was associated with either exposure or outcome. If these explorations suggest that assuming missingness of these variables is MAR is reasonable, I will continue to use a complete case analysis.

I was able to assess whether households entered poverty or lost income in the year prior to birth on only 62.2 and 57.9%, respectively, of the 6715 observations. These variables relied on availability of data on household income both in the year of birth and in the previous survey and were therefore more likely to be missing than variables from the year of birth. The analysis of this variable as a potential mediator should therefore be considered exploratory.

Chapter IV: Results

Descriptive statistics

Univariable analyses. Table 1 describes the mean (standard deviation [SD]) or number (proportion) of key variables in the study sample. Mean (SD) birth weight for gestational age percentile was 49.6 (29.3), mean (SD) maternal age was 26.8 (4.7), and mean (SD) net gestational weight gain was 10.7 (6.7). Approximately eleven percent of all births were SGA. Births to black and Hispanic mothers made up 24.9 and 19.0% of the sample, respectively, with the remainder of births in the non-black/non-Hispanic category. The majority (68.2%) of births was to mothers between 20-30 years old, and 27.4% were to mothers between 30-40 years. Births to mothers with <12 years education and those below the federal poverty level made up 20.1 and 23.4% of the sample, respectively. The majority of births was to women of normal pre-pregnancy BMI (67.1%) and occurred between 37-40 weeks gestation (74.3%). Women were primarily employed (48.3%) or keeping house (35.7%). One-third of women reported smoking in the year of the birth.

Exposure to labor market insecurity and labor market security during the first, second, and third trimesters characterized 5.4%, 5.7%, and 4.8% and 6.5%, 6.6%, and 6.8% of the births, respectively. Only 1.3% and 2.0% of pregnancies were exposed to labor market insecurity or security, respectively, in more than one trimester (data not shown).

Bivariable analyses

Exposure to labor market insecurity and birth weight percentile. Mean birth weight percentile was significantly lower among gestations exposed (vs. unexposed) to labor market insecurity in the first trimester (44.5 vs. 49.8, p<0.01). Mean birth weight percentile did not differ significantly between gestations exposed vs. unexposed to labor market insecurity in the second and third trimester (48.2 vs. 49.6, p=0.34 and 49.0 vs. 50.0, p=0.72, respectively).

Exposure to labor market security and birth weight percentile. Mean birth weight percentile was lower, although not significantly, among gestations exposed (vs. unexposed) to labor market security in the first trimester (47.3 vs. 49.7, p=0.10). Mean birth weight percentile did not differ significantly between gestations exposed vs. unexposed to labor market security in the second and third trimester (49.4 vs. 49.6, p=0.88 and 49.5 vs. 49.6, p=0.99, respectively).

Exposure to labor market insecurity and SGA. The proportions of SGA births were significantly higher among gestations exposed (vs. unexposed) to labor market insecurity in both the first and second trimester (16.1 vs. 11.0%, p<0.01, 14.4 vs. 11.0%, p=0.05, respectively). The proportion of SGA births did not differ significantly among gestations exposed vs. unexposed to labor market insecurity in the third trimester (9.0 vs. 11.3%, p=0.20).

Exposure to labor market security and SGA. The proportion of SGA births did not differ significantly among gestations exposed vs. unexposed to labor market security in the first, second, or third trimesters (11.2 vs. 11.2%, p=0.99, 10.3 vs. 11.3%, p=0.54, and 12.0 vs. 11.1%, p=0.60, respectively).

Box plots of birth weight percentile by labor market perturbation variables. Box plots of birth weight percentile by exposure to labor market insecurity did not demonstrate deviations from normality, skewness, or outliers (Figure 3a). The median and range of birth weight percentile for gestations exposed to labor market insecurity in the first trimester appeared lower compared to gestations unexposed in the first trimester. Box plots of birth weight percentile by exposure to labor market security also did not demonstrate deviations from normality, skewness, or outliers (Figure 3b). The median of birth weight percentile for gestations exposed to labor market security in the first trimester appeared slightly lower compared to gestations unexposed in the first trimester.

Temporal trends in labor market perturbation and birth weight for gestational age outcome variables. Figures 4a and 4b show the probability of exposure to labor market insecurity and security during the first, second, and third trimester among gestations in the study sample from 1982-2000. Probability of exposure to labor market insecurity in all three trimesters was greatest in 1982-1983, 1986, 1989-1992, and 1995-1996. Probability of exposure to labor market security in all three trimesters was greatest in 1984 and 1986, with smaller peaks in 1990, 1994, and 1998. Figures 5a and 5b show the mean birth weight percentile and proportion SGA over the study period. Mean birth weight percentile appeared to trend upward over the study period. The proportion SGA was highest between 1982 and 1986, with other high values seen in 1991, 1996 and 1998.

In unadjusted linear and logistic regression models, year of birth was significantly associated with exposure to both labor market insecurity and security as well as birth weight percentile and SGA ($p<0.01$). Year of birth was associated with a decrease in the probability of exposure to both labor market security and insecurity in all three trimesters, an increase in mean birth weight percentile, and a decrease in odds of SGA over the study period. These shared temporal trends suggested the need to control for a linear time trend (i.e., year of birth as a continuous variable) in multivariable models.

Aim 1 analyses

To address Aim 1, I examined the association between maternal exposure to state-level labor market perturbations (i.e., high labor market insecurity or security, in separate models) during each trimester of pregnancy and fetal growth, as measured by birth weight for gestational age percentiles.

Primary analysis

Exposure to labor market insecurity. Table 2 shows results from the multivariable model examining associations between exposure to labor market insecurity in each trimester and birth weight percentile outcomes (Model BW_A). Exposure to labor market insecurity in the first trimester was significantly associated with a decrease in birth weight for gestational age of 4.05 percentile points (95% CI = -6.87, -1.22), controlling for maternal age, race/ethnicity, education, marital status, poverty status, parity, and pre-pregnancy BMI and infant year of birth. Insecurity in the second and third trimesters was not significantly associated with birth weight percentile (β = -0.28, 95% CI = -3.01, 2.44 and β = 0.49, 95% CI = -3.06, 4.05, respectively).

Measures of association from individual characteristics of gestations were in the expected directions. Non-Hispanic black and Hispanic race/ethnicity, <12 years education, nulliparity, and underweight BMI were significantly associated with lower birth weights percentiles, while >12 years education, being married, and overweight and obese BMI were significantly associated with higher birth weight percentiles. After controlling for these individual-level covariates, year of birth was not significantly associated with birth weight percentiles.

Exposure to labor market insecurity in the first trimester was also significantly associated with higher odds of SGA (OR = 1.50, 95% CI = 1.21, 1.86), while insecurity in the second trimester was marginally associated with higher odds of SGA (OR = 1.28, 95% CI = 1.00, 1.65), and insecurity in the third trimester was not significantly associated with odds of SGA (OR = 0.75, 95% CI = 0.49, 1.13) (Model SGA_A).

Figure 6 demonstrates the difference in birth weight percentile associated with labor market perturbations in each trimester, and Figure 7 demonstrates the odds ratios for SGA associated with exposure to labor market insecurity in each trimester.

Exposure to labor market security. Exposure to labor market insecurity was not significantly associated with birth weight for gestational age percentile (Model BW_B) or odds of SGA (Model SGA_B) in any of the three trimesters (Table 3).

<u>Sensitivity analyses</u>

State of residence: additional analysis. I compared three sets of models to the primary analysis models, which used GEE to account for within-state correlation. These models were a) standard regression models using state indicator variables, b) GEE models accounting for within-mother correlation, and c) GEE models accounting for within-mother correlation with state indicator variables. In these models, estimates of association between exposure to labor market insecurity in all trimesters and birth weight percentile were attenuated (≤0.76 birth weight percentile points) but were of similar magnitude, direction, and statistical significance to estimates reported in the primary analysis (Table 4). Standard errors from these models were either similar or slightly larger (≤0.2 units) than the primary models. Odds ratios for SGA and corresponding standard errors did not change appreciably (Table 4). The non-significant associations between labor market security and birth weight percentile outcomes also did not change substantially under these sensitivity analyses (data not shown).

Shared temporal trends: additional analysis. Table 4 also demonstrates results of models using different methods to control for potential confounding by temporal trends shared by both exposure and outcome. Although the continuous year of birth variable was included in the primary models because of evidence that both exposure and outcome exhibited a temporal trend during the study period, estimates from models not including this variable were similar to those including it (Table 4).

Estimates of the association between labor market insecurity and birth weight percentile outcomes from models including year indicator variables were slightly attenuated (≤0.3 birth weight percentile points) but of similar magnitude, direction, and statistical significance to estimates reported in the primary analysis (Table 4). Odds ratios for SGA and corresponding standard errors did not change appreciably (Table 4).

Based on my visual inspection of Figures 3 and 4, which suggested that exposure to labor market perturbations was more frequent in the early years of the study period (1982-1986), while mean birth weight was lower and the probability of SGA was higher during these years, I also performed a sensitivity analyses for models BW_A and BW_B and SGA_A and SGA_B, including 4-5 year period indicator variables (1982-1986, 1987-1991, 1992-1996, 1997-2000). Estimates and standard errors from these models were similar to those from the primary analysis models (Table 4).

Estimates of association from models examining the association between labor market insecurity and residual values of birth weight percentile (after regression of this variable on state-by-year effects) were also similar to estimates from the primary analysis (Table 4). The non-significant associations between labor market security and birth weight percentile outcomes did not change appreciably under any of the analyses described above (data not shown).

Other measures of labor market perturbation. Positive residual values of the state monthly unemployment rates were not significantly associated with either birth weight percentile (Table 5) or odds of SGA (data not shown). Negative residual values were not significantly associated with birth weight percentile expect in the second month of gestation (Table 5) and were not associated with SGA in any month (data not shown). Labor market perturbations in the three months prior to pregnancy were also not associated with birth weight percentile outcomes (data not shown).

Additional individual covariates: Adjustment for maternal report of health limitations in the year of birth and maternal employment status did not substantially change estimates of association from models BW_A and BW_B and SGA_A and SGA_B (<0.1 birth weight percentile points and <0.05 change in OR). Health limitations and employment status were not significant predictors of birth weight percentile outcomes.

Aim 2 analyses

In Aim 2, I examined whether the association between labor market perturbations during pregnancy and birth weight for gestational age percentile differed by maternal characteristics. In the analysis for Aim 1 described above, I found a significant association between birth weight for gestational age percentile and only one labor market perturbation variable: exposure to labor market insecurity in the first trimester. I therefore explored potential effect measure modification of this association by maternal race/ethnicity, childhood SES, educational attainment, marital status, employment status, and poverty status. Table 6 shows the distribution of exposure to labor market insecurity in the first trimester by these potential effect modifiers and the mean birth weight percentile among these groups. Mean birth weight percentile was higher among unexposed women in all groups, except among unemployed women. Two-sample t-tests within these groups suggest that the difference in mean birth weight percentile among exposed and unexposed women was statistically significant (p<0.05) among non-Hispanic/non-Black women, women with average or high childhood SES, women with <12 years education, married women, those keeping house or out of the labor force, and women both above and below the federal poverty level.

In multivariable linear regression models of birth weight percentile, there was evidence of a statistically significant interaction between low maternal childhood SES and exposure to labor market insecurity in the first trimester (p-value for Wald test on interaction terms = 0.14). Among women with average or high childhood SES, exposure to labor market insecurity in the first trimester was associated with decreases in birth weight percentile of 5.52 (95% CI = -10.0, -1.04) and 8.66 points, respectively (95% CI = -14.04, -3.29) (Table 7). Among women with low childhood SES, however, exposure to labor market insecurity in the first trimester was not associated with a decrease in birth weight percentile (Table 7).

I also found evidence of a statistically significant interaction between maternal educational attainment and exposure to labor market insecurity in the first trimester (p-value for

Wald test on interaction terms = 0.18). Among women with < 12 years educational attainment, exposure to labor market insecurity in the first trimester was associated with a decrease in birth weight percentile of 9.22 points (95% CI = -15.77, -2.88) (Table 7). Among women with 12 years or >12 years educational attainment, exposure to labor market insecurity in the first trimester was not associated with birth weight percentile (Table 7).

The association between exposure to labor market insecurity in the first trimester and birth weight percentile also differed significantly by maternal employment status (p-value for Wald test on interaction terms = 0.04). Among women keeping house, exposure to labor market insecurity was associated with a decrease in birth weight percentile of 7.10 points (95% CI = -12.33, -1.87), and among women out of the labor force, exposure was associated with a decrease of 10.27 points (95% CI = (-18.82, -1.71) (Table 7). Exposure to labor market insecurity in the first trimester was not associated with a decrease in birth weight percentile among employed and unemployed women (Table 7).

I found no evidence of statistically significant interactions between exposure to labor market insecurity in the first trimester and maternal race/ethnicity, poverty status, or marital status in models of birth weight percentile. Although these interactions were not significant, some cells had small numbers of observations, and I therefore still report the effect estimates within these groups (Table 7). The difference in birth weight percentile comparing women exposed to labor market insecurity in the first trimester to unexposed women was smaller among women of Hispanic race/ethnicity compared to women of Black and non-Hispanic/non-Black race/ethnicity and larger among women below the federal poverty level compared to women above the federal poverty level.

Aim 3 analyses

In Aim 3, I explore whether the association between exposure to labor market insecurity during gestation and birth weight for gestational age percentile is mediated by individual economic change (i.e., maternal job loss, household entered poverty, and household income loss) or maternal pregnancy behaviors (i.e., smoking, first trimester prenatal care, and net gestational weight gain).

Table 8 shows the distribution of exposure to labor market insecurity in the first trimester by these potential mediators and the mean birth weight percentile among these groups. Several cells had small numbers once stratified by potential mediators, specifically exposed women with job loss, those whose household entered poverty or lost income, and those who did not utilize prenatal care in the first trimester. Mean birth weight percentile was higher among unexposed women in all groups. Two-sample t-tests within these groups suggest that the difference in mean birth weight percentile among exposed and unexposed women was *not* statistically significant among women with job loss, household entering poverty, or household income loss.

Tests for interaction between potential mediators and exposure. I first examined whether the exposure interacted significantly with any of the potential mediator variables in linear regression models. As in Aim 2, I examined potential interaction for only the significant association between exposure to labor market insecurity in the first trimester and birth weight percentile found in Aim 1. Exposure to labor market insecurity in the first trimester did not interact significantly with maternal job loss, household entering poverty, household income loss, first trimester prenatal care, or net maternal gestational weight gain. For these potential mediators, I therefore estimate the total and direct effects as well as the proportion explained, as described in Chapter III. Exposure to labor market insecurity in the first trimester interacted significantly with maternal smoking (p-value for interaction term <0.01), so I therefore report only the total effect and the direct effects at each level of smoking, as described in Chapter III.

Results of mediation analyses. None of the individual economic change variables was significantly associated with birth weight percentile. Inclusion of these variables in the regression models did not substantially change the estimate of association for exposure to labor market insecurity in the first trimester, and these variables explained <1% of the total effect of exposure to labor market insecurity in the first trimester on birth weight percentile (Table 9). First trimester prenatal care also was not significantly associated with birth weight percentile and explained <1% of the total effect (Table 9).

Each kg of net maternal gestational weight gain was associated with a 0.56 point (95% CI = 0.45, 0.67) increase in birth weight percentile. Including this variable in the model attenuated the association between exposure to labor market insecurity in the first trimester and birth weight percentile to -3.61 (95% CI = -6.29, -0.92), indicating that net gestational weight gain explained approximately 11% of this association (Table 9).

Table 9 also shows the direct effects of exposure to labor market insecurity in the first trimester, controlling for maternal smoking, among both women who reported smoking in the year of birth and those who did not. Among non-smokers, there was not a significant direct effect of labor market insecurity on birth weight percentile. Among smokers, exposure to labor market insecurity was associated with a decrease in birth weight of 7.40 percentile points (95% CI = -11.27, -3.52).

Missing data analyses

Investigation of missingness of exposure and outcome data. Gestations with missing data on labor market perturbations were significantly older, less likely to be below the federal poverty level, more likely to be nulliparous, more likely to have been in the original military sample, and more likely to be either black or Hispanic (data not shown). Gestations with missing data on birth weight percentile outcomes were significantly older, more likely to be overweight or obese, less likely to be nulliparous, and more likely to be black (data not shown).

The probability of exposure to labor market insecurity did not differ between gestations missing and not missing data on birth weight for gestational age outcomes (data not shown). Gestations missing (compared to those not missing) birth weight for gestational age outcomes were less likely to be exposed to labor market security in the first (3.1 vs. 6.5%, p <0.01) and second (3.9 vs. 6.6%, p=0.04) trimesters. Birth weight percentile outcomes did not differ between gestations missing and not missing data on labor market perturbations (data not shown).

Multiple imputation sensitivity analysis for missing covariates. Analyses using multiple imputation to impute missing data on maternal educational attainment, marital status, poverty status, and pre-pregnancy BMI demonstrated estimates of association were similar in magnitude, direction, and statistical significance to those from the non-imputed models. Specifically, exposure to labor market insecurity in the first trimester was associated with a decrease in birth weight percentile of 4.26 percentile points (95% CI = -7.30, -1.22).

Investigation of missingness of potential effect modifier and mediator data. Because maternal childhood SES was measured at baseline, I examined only other baseline variables, i.e., race/ethnicity or being in the economically disadvantaged or military sample, as potential predictors of missingness of childhood SES. Gestations missing maternal childhood SES were significantly more likely to be black or Hispanic and less likely to have been in the economically disadvantaged sample (data not shown). Gestations with missing data on poverty status were significantly older, more likely to be black or Hispanic, and less likely to have >12 years education (data not shown). Gestations with missing data on net maternal gestational weight gain were significantly older and less likely to be nulliparous (data not shown).

Probability of exposure to labor market insecurity or security did not differ between gestations missing and not missing data on childhood SES or net gestational weight gain (data not shown). Gestations missing (compared to those not missing) poverty status were less likely to be exposed to labor market insecurity and security in the first trimesters. Birth weight percentile outcomes did not differ between gestations missing and not missing data on poverty status or net gestational weight gain, but gestations missing data on maternal childhood SES had lower mean birth weight for gestational age percentile (data not shown).

Chapter V: Discussion

In this dissertation, I examined the association between exposure to perturbations to labor market security during gestation and fetal growth, as measured by birth weight for gestational age percentile. This research question stems from the conceptual framework developed in Chapter I, which proposes that unexpected changes to the human ecology, i.e. perturbations, may result in unexpected behavioral and biological responses in humans and that such responses will be conserved by natural selection if they are adaptive. Based on this framework, I hypothesized that reductions in fetal growth would occur in response to ecological perturbations during gestation. I used months of unexpectedly high labor market insecurity and security as contemporary measures of ecological perturbation and examined fetal growth as a theoretically and biologically plausible response to these perturbations.

Summary of findings

Aim 1. Examining associations between exposure to unexpectedly high labor market insecurity and security (i.e., labor market perturbations) in each trimester and fetal growth, I found that exposure to labor market insecurity during the first trimester of gestation was significantly associated with a decrease in birth weight for gestational age of approximately four percentile points and a 50 percent increase in odds of SGA. Exposure to labor market insecurity in the second trimester was also associated with a marginally significant 28 percent increase in odds of SGA. Exposure to labor market insecurity in the third trimester was not significantly associated with birth weight percentile outcomes, and exposure to unexpectedly high labor market security was not associated with birth weight percentile outcomes in any trimester.

Aim 2. In Aim 2, I examined differences in the association between labor market perturbations during pregnancy and birth weight for gestational age percentile by maternal race/ethnicity, childhood SES, educational attainment, marital status, employment status and poverty status. The difference in average birth weight percentile among gestations exposed vs. unexposed to labor market insecurity in the first trimester was significantly larger among women with < 12 years education compared to those with 12 or more years of education and among women keeping house or out of the labor force compared to employed women. Associations also varied significantly by maternal childhood SES: the difference in birth weight percentile comparing gestations exposed vs. unexposed to labor market insecurity in the first trimester was largest (and significant) among women of high childhood SES, second largest (and significant) among women with average childhood SES, and smallest and non-significant among women of low childhood SES.

The association between exposure to labor market insecurity in the first trimester and birth weight percentile did not differ significantly by race/ethnicity, marital status, or poverty status. However, the association between exposure to labor market insecurity in the first trimester was (non-significantly) smaller among Hispanic women compared to non-Hispanic black and white women and among women above, compared to below, the federal poverty level.

Aim 3. In Aim 3, I explored whether the association between labor market insecurity in the first trimester of gestation was mediated by individual economic change (i.e., maternal job loss, household entered poverty, and household income loss) or maternal pregnancy behaviors (i.e., smoking, first trimester prenatal care, and net gestational weight gain).

The association between exposure to labor market insecurity in the first trimester of gestation and birth weight percentile was not mediated by maternal individual economic change (maternal job loss or household income loss) or by utilization of prenatal care in the first trimester. Approximately 11 percent of the association was mediated by net maternal gestational weight gain. I found a significant interaction between exposure to labor market insecurity in the first trimester and maternal smoking in the year of birth: the difference in birth weight percentile comparing exposed vs. unexposed gestations was significant only among women who smoked in the year of the birth.

Implications of findings

Main findings and subgroup differences. Overall, findings from this study support my hypothesis that fetal growth responds to a contemporary ecological perturbation, i.e., unexpectedly high labor market insecurity. The finding that associations between exposure to labor market insecurity and birth weight percentile were stronger among women with <12 years education and those keeping house or out of the labor force suggests that these women may be more vulnerable to economic perturbations. Less educated women may experience a disproportionate burden of labor market insecurity if, for example, they, their families, or their communities are more likely to experience job loss compared to women with more education. Research has shown that both females and males between 20 and 35 with less than 12 years education were more likely to experience job loss during the 1980s and early 1990s than their counterparts with 12 or more years of education.[138] This burden of job loss less educated populations may result in individual loss of resources or increased stress and anxiety among. Women with less education may also respond differently to high labor market insecurity due to differences in resources, social support, or coping mechanisms.

Women who are out of the labor force are likely either disabled or discouraged workers. These women, as well as those who are keeping house, may rely more on spouses or other family members for income and be therefore disproportionately affected when these wage earners either lose their jobs or are threatened with job loss.

These findings could shed light on one potential determinant of the higher risk of adverse birth outcomes seen in women with less education and lower occupational status.[2] That is, if these groups are more vulnerable to economic or other ecologic perturbations, they may exhibit lower mean birth weights over time. It is important to note, however, that some of these subgroups were very small (e.g., n=333 unemployed women), and these findings need to be confirmed in datasets with larger sample sizes for subgroups.

The finding that the association between labor market insecurity and birth weight percentile was small and non-significant among Hispanic women reflects other research demonstrating weaker associations between socioeconomic factors and birth outcomes among Hispanics than among non-Hispanic blacks.[2] Hypotheses put forward to explain this "paradox" include that Hispanic communities have more social support or that Hispanics living in the U.S. are a healthy subsample of the general population in their sending countries.[139] I hesitate to interpret these findings or make such hypotheses in my own data for several reasons. First, the association between labor market insecurity and birth weight percentile in this group did not differ significantly from that among non-Hispanic blacks and whites. Second, the number of "exposed" Hispanic gestations was small, and estimates from this group may not be stable.

Further, I was not able to divide the Hispanic births into subgroups among which birth outcomes have been shown to differ (e.g. foreign-born vs. native-born, country of origin).[5] These data also did not allow for potentially informative explorations of interactions between race/ethnicity, education, age, and other variables. My results do suggest that such analyses would be worth examining in larger datasets, such as vital statistics data, which would have larger sample sizes that could be stratified by race and ethnicity and which could be used to examine race-by-age or race-by-education interactions.

My finding that the association between exposure to labor market insecurity and birth weight percentile was highest among women with high childhood SES and non-significant among women with low childhood SES was unexpected and has several potential explanations. First, once stratified by childhood SES, these data may have been limited by the small number of exposed women at each level, making these estimates potentially unstable. On the other hand, the childhood SES variable may represent characteristics of women that do in fact affect vulnerability to labor market insecurity. Women of high childhood SES (or their spouses or partners) may be more likely to be employed in the labor market and therefore more concerned about or aware of perturbations in the labor market. Research has demonstrated that childhood SES is strongly associated with adult education and wage attainment, both of which are correlated with employment.[140,141] Women of high childhood SES may also differ in terms of social support or other resources that I was unable to assess. In order to fully understand these findings, further research is needed on the meaning of various measures of childhood SES and the relations between childhood and early adulthood SES and the response of fetal growth to economic perturbations.

My analysis of maternal smoking as a potential mediator of the association between exposure to labor market insecurity in the first trimester and birth weight percentile found that this variable interacted significantly with exposure. Women who smoked in the year of birth experienced a larger reduction in birth weight percentile following exposure to labor market insecurity than non-smokers. From this data, I cannot determine whether women smoked during pregnancy or quit before pregnancy, i.e. I cannot assess the temporal order of smoking and exposure to labor market insecurity. Smokers may represent another subgroup with higher vulnerability to labor market insecurity, potentially due to lower baseline health or other characteristics associated with smoking, such as self-esteem, psychosocial stress, or mental health.[142,143] Alternatively, exposure to labor market insecurity may make women more likely to smoke during pregnancy and cause greater reductions in fetal growth in those that do.

<u>Timing of exposure during gestation.</u> The finding that birth weight for gestational age percentile outcomes were more strongly associated with labor market insecurity in the first trimester could reflect changes to early gestational physiological processes affecting fetal growth, such as implantation or trophoblast invasion, which may be affected by maternal diet or stress and subsequently affect placental transfer of nutrients to the fetus.[72-74] Other research suggests that the psychological or physiological stress response remains active in early pregnancy but becomes blunted as pregnancy advances.[69]

It is also possible that effects of unexpectedly high unemployment on the population are not felt until several months later, in which case these early perturbations could be affecting fetal growth later in gestation. My finding that exposure to labor market insecurity in the three months prior to pregnancy was not associated with birth weight percentile makes this a less plausible explanation. A final possibility is that maternal responses to perturbations (e.g., changes diet or increases in stress hormones) take several months to impact gestational health, in which case perturbations later in gestation may have weaker effects.

Measures of perturbation to labor market security. These findings support my hypothesis that exposure to unexpectedly high labor market insecurity but not security is associated with reduced fetal growth. Based on the ecologic-evolutionary framework described in Chapter I, I hypothesized that high labor market insecurity (i.e., unexpectedly high unemployment) would simulate ecological perturbations seen in evolutionary history that threatened availability of resources (e.g., nutrition) for mothers and offspring, eliciting an adaptive response conserved from evolutionary history, i.e. reduced fetal growth.

The finding that labor market security is not associated with fetal growth may result because unexpectedly low unemployment does not correlate to an ecological perturbation such as those experienced in our evolutionary history and therefore does not elicit a corresponding conserved response in fetal growth. This finding may also mean that individuals in the labor market are less aware of lower-than-expected unemployment, perhaps due to less media coverage.

These findings also suggest that less extreme perturbations to labor market security, as measured by the positive and negative residuals of the unemployment rate, were not associated with birth weight percentile outcomes. Although the negative residual value was associated with birth weight for gestational age percentile in the second month of pregnancy, I suggest that this marginally significant finding (p=0.05) is not meaningful given the large number of tests in this model. These findings imply a threshold effect whereby a certain level of perturbation is required to elicit a fetal growth response. Future research should examine other levels of perturbation to pinpoint such a threshold.

Pathways between labor market insecurity and birth weight percentile. This analysis explored a subset of the possible pathways through which labor market perturbations could affect birth weight percentile outcomes. The finding that the association between exposure to labor market insecurity in the first trimester and birth weight percentile is not mediated by individual economic change such as maternal job loss or household income loss suggests that this labor market insecurity affects even the gestations of women whose individual employment or economic situation remains unchanged. This finding suggests that unexpectedly high labor market insecurity represents a *population-level* stressor. Previous research has also shown that rates of LBW increased following threatened lay-offs that were never realized, suggesting a similar, population-level stress, mechanism.[122] In this analysis, however, I was unable to measure job loss in the household (e.g., father or other income-earner); it is possible that some of the association between macro-level economic change and individual birth outcomes is mediated by job loss, just not *maternal* job loss. Further, the variables for household income loss and entering poverty measured changes in household income between the survey closest to the birth and the previous survey. These changes may therefore have occurred before, after, or during pregnancy; more accurate measurement of income change during pregnancy may have produced different results. Finally, it should be noted that the numbers of women exposed to labor market insecurity and experiencing individual economic change were very small (Table 8), and these findings should be interpreted with caution.

An intriguing finding of this research is that net maternal gestational weight gain (the difference between total weight gain and birth weight) mediates approximately 11% of the association between exposure to labor market insecurity and birth weight percentile. This means that following exposure to labor market insecurity some women gain less weight than they might have otherwise, resulting in lower birth weight for gestational age percentile. Previous research in non-pregnant women suggests that individuals may spend more time on physical activity and reduce BMI when employment rates decrease. [83,86] Future research should further explore the role of maternal nutrition in mediating associations between ecologic perturbations and birth weight outcomes.

I also found that the association between exposure to labor market insecurity in the first trimester and birth weight percentile was not mediated by maternal utilization of prenatal care in the first trimester. Due to the statistically significant interaction between the exposure and maternal smoking, I was unable to assess the proportion of the total effect of exposure mediated by maternal smoking, but further research should attempt to do this using more advanced statistical methods.[134]

These findings leave open the possibility that additional pathways connecting labor market perturbations and birth weight percentile exist. Such pathways may include other, unmeasured behavioral changes, e.g. physical activity, diet, or prescription or illegal drug use. Physiological responses to labor market perturbation such as activation of the HPA axis in the stress response[58], reduction in BMR[46], changes in insulin sensitivity[46], or other unexplored mechanisms may also represent pathways between exposure to labor market insecurity and birth weight percentile. While estimation of some of these pathways may help explain the reduction in fetal growth seen in this study, it is important to note that some mediators could also increase fetal growth. If, for example, women reduce smoking during economic downturns—as previous research has suggested in non-pregnant populations [86]—this could increase fetal growth in some pregnancies while reduced weight gain, stress, or other factors reduce fetal growth in other pregnancies. Estimates of effects of labor market perturbations on fetal growth could therefore be underestimated because pathways lead to effects in opposite directions.

Contributions to existing literature

This research differs from much previous research examining determinants of birth weight outcomes. Research has traditionally focused on identifying individual-level factors such as maternal age, weight gain, and smoking.[7] Although many such individual-level determinants have been identified, much of the variation in birth weight outcomes—that is, differences between populations and over time—remains after adjusting for the effects of these risk factors, and little research has explored the *determinants* of these risk factors. These gaps in our current understanding suggest the need to examine more macro-level ecological determinants of birth outcomes. Recent research has in fact examined macro-level determinants such as neighborhood-level poverty, social disorder, and racial segregation.[20,144] Much of this research has demonstrated associations between suboptimal ecological circumstances—e.g., neighborhood poverty, racial segregation—and reduced birth weight, but debate remains as to whether these factors affect birth weight above and beyond individual-level factors.[20] Although research on these static measures of the human ecology may help explain observed differences in birth weight between populations in the U.S., this literature does not contribute to our understanding of temporal changes in birth weight (overall or within certain populations). In this dissertation, I examine associations between perturbations to the human ecology and fetal growth, a line of inquiry that may shed light on population-level processes contributing to both between-population differences in birth weight outcomes as well as between- and within-population temporal trends.

As described in Chapter II, several previous studies have also examined associations between birth outcomes and ecological perturbations such as earthquakes and terrorist attacks, reporting mixed results but providing preliminary evidence that birth outcomes may respond to ecological perturbations. A small number of studies have specifically examined associations between macro-level economic change and birth outcomes. However, this literature has produced decidedly mixed findings that differ by measurement of economy and birth outcome, time period and population, and methodology. This study contributes to this field by using the conceptual framework described in Chapter 1 to select measures of economic perturbation and birth outcome based on theory and biological plausibility.

My findings are similar to those from the most rigorous studies reviewed in Chapter II, which showed higher rates of LBW following both higher than expected male employment[123] and threats to labor market security[122]. Although previous literature has documented associations between individual-level economic change and birth outcomes[38,39,125], I did not find evidence in this study that maternal job loss or household income loss were directly associated with birth weight percentile in models that included macro-level labor market insecurity, individual characteristics, and year of birth.

Methodological considerations

This research contributes not only conceptually and substantially, but also methodologically, to the literature on ecological perturbations, specifically economic perturbations, and birth weight outcomes. First, this study employs a multilevel design to examine the association between macro-level economic perturbations and individual-level birth weight outcomes, enabling me to examine potential confounding and effect modification by individual-level maternal characteristics and potential mediation by maternal job loss, household income changes, and maternal behaviors during pregnancy. To my knowledge, no previous research on the economy and birth outcomes has explicitly examined these individual variables as confounders, effect modifiers, or mediators.

This study uses birth weight for gestational age percentile as the primary outcome, whereas most previous studies have examined either birth weight, LBW, or preterm birth. Whereas birth weight and LBW outcomes conflate effects on fetal growth and length of gestation, birth weight for gestational age is the closest approximation of fetal growth that is possible with the birth outcome variables reported in NLSY and other survey data. As discussed in Chapter I, I chose to focus on fetal growth, instead of length of gestation or preterm birth because of its theoretical and biological plausibility as an aspect of gestation that would respond to ecologic perturbation.

Measures of economic perturbation have also varied widely in previous studies. I used rigorous ARIMA models to estimate the expected value of the state unemployment rate in each month and then identified months in which the observed unemployment rate was statistically significantly above or below this expected value (labor market insecurity and security, respectively). This method produces more meaningful economic measures than comparing raw or seasonally adjusted unemployment rates because it takes into account all potential autocorrelation in the unemployment rate. My definition of labor market perturbations is also based on theoretical and empirical research in ecology and psychology suggesting that the "unexpectedness" of environmental stimuli constitutes an important potential determinant of health.

I used the monthly unemployment rate in maternal state of residence to measure the security of the labor market during gestations in the NLSY79 data. Choice of state as the unit of analysis was motivated by evidence that the unemployment rate at the state level is associated with anxiety and mood and because the state unemployment rate can be measured with more precision and is more likely to be reported in the media compared to local unemployment rates. Use of the monthly unemployment data allowed me to more precisely define gestations as exposed or unexposed to labor market perturbation in the first, second, or third trimester. Previous studies examining the association between unemployment and birth outcomes have often used annual data on the unemployment rate[45,124], which makes it difficult to determine whether observed changes in birth outcomes result from effects of the economy on selection of mothers into pregnancy or on gestational health itself. I found that labor market perturbations in the three months prior to conception were not associated with birth weight for gestational age percentile, suggesting that my findings were due to changes to gestational health, not selection.

In these analyses, I included individual-level characteristics of gestations (maternal age, race/ethnicity, education, marital status, poverty status, and parity) as control variables because of my *a priori* hypothesis that, as the NLSY79 cohort aged, characteristics of gestations would also change. Adjustment for individual-level characteristics of gestations did not substantially change the association between exposure to labor market perturbations and birth weight percentile outcomes. This suggests that these individual characteristics, which have been shown to be associated with birth weight outcomes, are not strongly associated with exposure to labor market perturbations.

In this sample, the probability of exposure to labor market security and insecurity decreased with year of birth in this sample, while birth weight for gestational age percentile increased with year of birth. In the general US population, birth weight for gestational age appears to have increased in the U.S. from 1980-1990 and to have decreased between 1990 and the present.[7] In the NLSY79 sample, the overall increase is likely due to the fact that mothers giving birth later in the study period were more likely to be white, well-educated, married, etc. I explored several ways of controlling for potential confounding by these shared temporal trends. Controlling for a linear time trend (year of birth variable) slightly attenuated associations between exposure to labor market insecurity and birth weight outcomes. This suggests that the two variables did share a general secular trend (affecting all states), but that this trend did not account for the discovered associations. In fact, the linear time trend was no longer a significant predictor of birth weight percentile after controlling for individual characteristics of births that would have changed as the NLSY79 sample aged.

Although visual inspection of the data (Figures 3a and 3b) suggested that some years or periods may have shared high or low values of both labor market perturbation and birth weight percentile variables, models including year and period indicator variables did not differ substantially from primary models. Results from models of the residuals of birth weight percentile based on regressions on state by year indicator variables also did not differ substantially from primary analyses. These sensitivity analyses suggest that the association between exposure to labor market insecurity and birth weight percentile was not confounded by temporal patterns shared by exposure and outcome.

Findings from Aim 1 were also robust to sensitivity analyses exploring alternate methods of accounting for within-state and within-mother correlation (GEE models) as well as potential confounding by state (state indicator variable models). Adjustment for maternal general health also did not substantially affect findings. It should be noted that this variable only measured health limitations that would have prevented the mother from working—complications of pregnancy were not measured in this data. Maternal complications of pregnancy (e.g., gestational diabetes, preeclampsia) may represent one unmeasured pathway by which exposure to labor market insecurity affects birth weight percentile outcomes.

The length (approximately 20 years) and large sample size of NLSY79 ensured ample variation in state economies over the study period. The NLSY79 sample, moreover, represents a diverse group of U.S. women and has a high retention rate over the study period (77.5% as of 2002). This dataset has several important limitations for this research, however. First, the self-reported nature of the data presents the potential for bias if women's ability to accurately recall their infants' birth weight or gestational age is not random. Accuracy of length of gestation measures may depend, for example, on the method of estimation used (e.g., last menstrual period, ultrasound, or clinical estimates), for which I did not have data. Recent studies have shown, however, that estimates based on LMP differ from ultrasound estimates by <3 days.[117,118] It is also likely that recall or measurement error in these variables is non-differential with respect to economic contraction and that any bias would be towards the null. Although my study sample included 6,715 gestations, many subgroup analyses (effect modification and mediation) were limited by small sample sizes. Some categories included less than 1000 women, such as those losing jobs, unemployed, or out of the labor force, making these estimates potentially unstable.

Several of the variables used in this analysis may have not perfectly represented the underlying construct I attempted to measure. First, in order to obtain state of residence on as many women as possible around the time of their pregnancy and birth, I used data from two years prior to and following birth (from 1994-2000, NLSY participants were only surveyed every two years.) This may have led to imputation of incorrect values for state of residence that could actually have been influenced by either economic shocks or birth outcomes, e.g. if the woman chose to move because of an economic shock or birth outcome. Second, there may be issues with using maternal gestational weight gain in models of birth weight for gestational age because both the weight gain and the outcome are dependent on gestational age. Findings from models of mediation by maternal gestational weight gain should therefore be interpreted with caution.

This dataset is also limited by missing data on birth weight, length of gestation, individual characteristics of gestations, individual economic variables, and maternal pregnancy behaviors. As with any survey dataset, participants may chose not to respond to certain questions, may not participate in some surveys, or may be lost to follow-up. My exploration of missingness of exposure to labor market perturbation and birth weight percentile variables demonstrated that missingness of both variables was predicted by observed values of variables included in the analysis, i.e. "missing at random" (MAR). Little and Rubin state that data that is MAR can be analyzed using complete case analysis (i.e., only analyzing the set of observations with no missing values), as I have done, without inducing bias.[137] It is impossible, however, to ascertain that data are in fact MAR. Missingness of exposure and/or outcome could depend on unobserved variables, i.e. those not measured by NLSY79, such as personality or mental health characteristics of the mother, which may affect follow-up or response to surveys.

I did not find evidence that the probability of missing data on labor market insecurity was associated with birth weight percentile or vice versa, providing further support that the main findings are not biased by missing exposure and outcome observations. Although gestations missing (compared to those not missing) birth weight for gestational age outcomes were less likely to be exposed to labor market security in the first and second trimesters, findings did not indicate any association between labor market security and birth weight outcomes. Results from analyses using multiple imputation for missing data on maternal educational attainment, marital status, poverty status, and pre-pregnancy BMI did not differ substantially from results using missing indicator variables, suggesting that missing data on covariates also did not bias these findings.

In general, missingness of potential effect modifier and mediator variables was also associated with observed values of variables included in the analysis, e.g. maternal age, race/ethnicity, educational attainment, and poverty status, suggesting that these variables are also MAR. Gestations missing data on poverty status were less likely to be exposed to labor market insecurity and security in the first trimester. This was likely a result of births later in the study period being more likely to have missing data and also being less likely to be exposed to labor market perturbations. Controlling for year of birth should mitigate some of the potential bias due to this association. Gestations missing childhood SES also had, on average, lower birth weight than gestations with data on childhood SES. The associations between missingness of childhood SES and poverty status and values of the exposure or outcome suggest that there may be some bias in the analyses of these variables as effect modifiers; results from these analyses should be interpreted with caution. Analyses of mediation by household change to poverty or income loss were conducted only in a subset of women with data on these variables (62.2 and 57.9% of the sample, respectively) and should therefore be considered exploratory.

Future directions

The research described in this dissertation makes a novel contribution to the field of research interested in understanding the macro-level, ecological determinants of fetal growth. Yet, much further work is needed to fully understand the association between perturbations to the labor market and fetal growth and to apply this research to understanding the differences in birth outcomes between populations and over time in the U.S. and elsewhere.

Future research should utilize larger vital statistics records to examine the extent to which the between- and within-populations differences and trends in birth weight outcomes can be explained by labor market perturbations. Research should also examine other ways of measuring labor market security and perturbations to the economy. This study, for example, used a conservative definition of unexpectedly “high” labor market insecurity; a less stringent definition might result in different findings. Examining whether or not labor market perturbations occurred during already secure or insecure periods (e.g., periods of low or high unemployment) may also be important, if populations are more vulnerable to perturbations when the labor market is already suboptimal. Other economic indicators, e.g. consumer prices, wages, or gross domestic product, could also be explored.

Much additional research, especially in larger datasets, could explore interactions between maternal characteristics, exposure to labor market insecurity, and birth outcomes. Prior studies have shown, for example, that younger black mothers have better birth outcomes compared to white mothers than older black mothers, suggesting that a race-by-age-by-exposure interaction may provide additional insight into which groups are more vulnerable to labor market perturbations. Data also show that, within Asian and Hispanic populations, birth outcomes differ by country of origin, but this study was only able to examine race/ethnicity as a three-category variable.

Future research should also pursue other potential mediators of the discovered association between exposure to labor market insecurity and birth weight percentile. More detailed data on maternal pregnancy behaviors and changes in family economic status during pregnancy, especially in larger datasets, could help elucidate these pathways. Although data may be difficult to obtain, information on maternal self-reported stress or stress biomarkers, BMR, or insulin sensitivity might also help elucidate mechanisms.

Finally, although this study was informed by the evolutionary theory described in Chapter I, it did not attempt to assess whether the observed reduction in fetal growth following labor market perturbations was in fact a conserved *adaptive* response. To pursue this question, additional data is needed on the health and reproductive fitness over the lifecourse of the infants in the study. Although NLSY79 has followed up some of the births between 1994 and the present, the sample size and length of follow-up will not likely facilitate such an analysis at this time. As this sample of children and young adults ages, however, we may be able to utilize data on their fertility to better examine such questions.

Overall, this research demonstrates how conceptualizing the population-level determinants of birth outcomes from an ecological-evolutionary framework may generate novel research questions that can begin to improve our understanding of the unexplained differences in birth outcomes in the U.S. between populations defined by race/ethnicity, socioeconomic status, and geography and the within- and between-population temporal trends.

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Tables and Figures

Table 1. Characteristics of gestations in study sample: singleton births between 1982 and 2000 to women in National Longitudinal Survey of Youth 1979 with available data on birth weight, length of gestation, and state of maternal residence (n=6715).

	Mean (SD)
Birth weight for gestational age percentile	49.6 (29.3)
Maternal age	26.8 (4.7)
Net maternal gestational weight gain	10.7 (6.7)
(missing = 145)	
	n (%)
Exposed to labor market insecurity	
Trimester one	360 (5.4)
Trimester two	383 (5.7)
Trimester three	321 (4.8)
Exposed to labor market security	
Trimester one	437 (6.5)
Trimester two	445 (6.6)
Trimester three	459 (6.8)
Small for gestational age	754 (11.2)
Maternal age	
<20	279 (4.2)
20-30	4577 (68.2)
30-40	1842 (27.4)
>=40	17 (0.3)
Maternal race/ethnicity	
Non-Black/non-Hispanic	3764 (56.1)
Black	1674 (24.9)
Hispanic	1277 (19.0)
Maternal educational attainment	
(missing = 132)	
< 12 years	1324 (20.1)
12 years	2838 (43.1)
> 12 years	2421 (36.8)
Mother married (missing = 126)	3930 (59.6)

Mother below federal poverty level	
(missing = 739)	1397 (23.4)
Nulliparous mother	2494 (37.1)
Maternal pre-pregnancy BMI	
(missing = 810)	
<18.5	470 (8.0)
18.5-24.9	3961 (67.1)
25.0-29.9	934 (15.8)
>=30	540 (9.1)
Maternal health limitation reported in year of birth	
(missing = 1121)	765 (13.7)
Length of gestation	
Very preterm (<32 weeks)	100 (1.5)
Preterm (32-36 weeks)	699 (10.4)
Term (37-40 weeks)	4990 (74.3)
Postterm (>40 weeks)	926 (13.8)
Childhood socioeconomic status (father's level of education)	
(missing = 971)	
Low (< 12 years)	2574 (44.8)
Average (12 years)	1940 (33.8)
High (> 12 years)	1230 (21.4)
Maternal employment status	
(missing = 649)	
Employed	2928 (48.3)
Unemployed	333 (5.5)
Keeping house	2166 (35.7)
Out of the labor force	639 (10.5)
Maternal smoking in the year of birth	
(missing = 16)	2023 (30.2)
Utilization of prenatal care in first trimester	
(missing = 214)	5370 (82.6)
Maternal job loss during pregnancy	432 (6.4)
Household entered poverty during year of birth	
(missing = 2538)	317 (7.6)
Household income loss during year of birth	
(missing = 2830)	1520 (39.1)

Table 2. Multivariable associations between exposure to labor market insecurity during the first, second, and third trimesters of gestation and birth weight for gestational age percentile with individual-level covariates and adjustment for linear time trend. [1,2]

	Difference in mean birth weight percentile (95% CI)
Labor market insecurity	
First trimester	-4.05 (-6.87, -1.22)
Second trimester	-0.28 (-3.01, 2.44)
Third trimester	0.49 (-3.06, 4.05)
Maternal age (years)	-0.26 (-0.68, 0.17)
Non-Hispanic black (vs. Non-Hispanic white)	-11.36 (-14.05, -8.67)
Hispanic (vs. Non-Hispanic white)	-3.26 (-5.93, -0.59)
<12 years education (vs. 12 years)	-2.90 (-5.52, -0.29)
>12 years education (vs. 12 years)	3.11 (1.50, 4.71)
Married	4.06 (2.40, 5.73)
Below federal poverty level	-2.03 (-4.33, 0.27)
Nulliparous	-4.53 (-5.99, -3.06)
BMI <18.5 (vs. 18.5-24.9)	-5.20 (-8.83, -1.58)
BMI 25.0-29.9 (vs. 18.5-24.9)	4.63 (2.28, 6.97)
BMI >30.0 (vs. 18.5-24.9)	9.56 (7.29, 11.83)
Year of birth	0.27 (-0.06, 0.59)

[1]Estimates from generalized estimating equations

[2]Models additionally adjusted for sampling characteristics (economically disadvantaged at enrollment and military sample)

Table 3. Multivariable associations between exposure to labor market security and labor market security during first, second, and third trimesters of gestation and birth weight for gestational age percentile and odds of small for gestational age (SGA)[1]

	Difference in mean birth weight percentile (95% CI)	**Odds ratio for SGA (95% CI)**
Labor market security		
First trimester	-1.00 (-4.37, 2.37)	0.93 (0.71, 1.23)
Second trimester	0.94 (-1.44, 3.32)	0.84 (0.63, 1.12)
Third trimester	1.32 (-1.22, 3.86)	1.03 (0.76, 1.40)

[1]Estimates from generalized estimating equations adjusted for maternal age, race/ethnicity, educational attainment, marital status, poverty status, parity, year of birth, and sampling variables.

Table 4. Comparison of estimates of association and standard errors (SE) from multivariable models[1]

Model specification	Difference in mean birth weight percentile (SE)			Odds ratio for SGA (SE)		
	Trimester One	Trimester Two	Trimester Three	Trimester One	Trimester Two	Trimester Three
Primary analysis model (GEE by state with continuous variable for year of birth)	-4.05 (1.44)	-0.28 (1.39)	0.49 (1.81)	1.50 (0.16)	1.28 (0.17)	0.75 (0.16)
Confounding/correlation within states/mothers						
State indicator variables	-3.94 (1.56)	-0.19 (1.51)	0.70 (1.63)	1.51 (0.24)	1.30 (0.21)	0.74 (0.15)
GEE by mother	-3.50 (1.44)	-0.82 (1.36)	0.51 (1.43)	1.46 (0.22)	1.31 (0.20)	0.75 (0.15)
GEE by mother with state indicator variables	-3.29 (1.43)	-0.65 (1.37)	0.88 (1.42)	1.51 (0.16)	1.30 (0.18)	0.74 (0.16)
Confounding by time (all GEE by state)						
No control for time	-4.38 (1.54)	-0.56 (1.50)	0.08 (1.63)	1.51 (0.16)	1.29 (0.17)	0.75 (0.16)
Year of birth indicator variables	-3.79 (1.38)	-0.18 (1.41)	0.39 (1.86)	1.49 (0.16)	1.28 (0.17)	0.74 (0.16)
5-year period of birth indicator variables	-4.00 (1.40)	-0.26 (1.39)	0.57 (1.87)	1.50 (0.16)	1.28 (0.17)	0.74 (0.16)
Residuals of birth weight for gestational age percentile[2]	-4.06 (1.39)	-0.40 (1.32)	0.48 (1.85)			

[1]All models adjusted for maternal age, race/ethnicity, educational attainment, marital status, poverty status, parity, and sampling variables

[2]From regression model of birth weight percentiles on state-by-year of birth interaction terms

Table 5. Multivariable associations between positive and negative monthly residual (observed – expected) values of unemployment and birth weight for gestational age percentile.[1]

Month of gestation	Difference in mean birth weight percentile (95% CI)	
	Positive residual	Negative residual
1	-1.17 (-5.46, 3.12)	-2.52 (-6.77, 1.73)
2	-0.68 (-4.42, 3.07)	-5.79 (-11.53, -0.04)
3	0.75 (-3.57, 5.06)	1.65 (-2.94, 6.25)
4	2.86 (-1.51, 7.24)	1.37 (-3.53, 6.27)
5	-3.28 (-7.36, 0.8)	-1.7 (-7.88, 4.48)
6	-2.75 (-7.08, 1.58)	-0.37 (-4.78, 4.03)
7	1.87 (-2.39, 6.14)	0.25 (-3.06, 3.56)
8	2.48 (-1.72, 6.68)	3.59 (-0.29, 7.48)
9	-1.52 (-6.16, 3.12)	-0.49 (-4.92, 3.95)

[1]Estimates from generalized estimating equations adjusted for maternal age, race/ethnicity, educational attainment, marital status, poverty status, parity, year of birth, and sampling variables.

Table 6. Distribution of exposure to labor market insecurity in first trimester by potential effect modifier variables and mean (SD) birth weight for gestational age percentile by exposure status within categories of potential effect modifiers

Potential effect modifier	Labor market insecurity in first trimester (1=exposed, 0=unexposed)	Number in category	Mean (SD) birth weight for gestational age percentile	p-value[1]
Race/ethnicity				
Non-Black/non-Hispanic	0	3556	53.2 (28.7)	0.0018
	1	208	46.8 (30.2)	
Black	0	1578	41.6 (29.2)	0.1659
	1	96	37.3 (29.1)	
Hispanic	0	1221	50.7 (28.8)	0.5031
	1	56	48.1 (28.8)	
Childhood socioeconomic status (father's level of education)				
< 12 years	0	2426	48.9 (29.6)	0.1678
	1	148	45.5 (30.9)	
12 years	0	1835	50.7 (29.2)	0.0177
	1	105	43.8 (30.1)	
> 12 years	0	1168	53.4 (28.0)	0.0033
	1	62	42.6 (28.1)	
Educational attainment				
Low (< 12 years)	0	1224	45.2 (29.5)	0.0006
	1	100	34.7 (28.2)	
Average (12 years)	0	2704	49.2 (29.6)	0.2341
	1	134	46.1 (31.1)	
High (> 12 years)	0	2300	53.0 (28.5)	0.3965
	1	121	50.7 (27.9)	
Marital status				
Unmarried	0	2493	43.8 (29.4)	0.2814
	1	166	41.3 (30.3)	
Married	0	3741	53.8 (28.6)	0.0022
	1	189	47.2 (29.2)	
Employment status				

Employed	0	2762	51.3 (28.7)	0.0810
	1	166	47.3 (28.3)	
Unemployed	0	311	44.1 (30.0)	0.3496
	1	22	50.3 (33.8)	
Keeping house	0	2042	49.1 (29.4)	0.0018
	1	124	40.7 (29.8)	
Out of labor force	0	605	47.1 (29.9)	0.0238
	1	34	35.1 (32.9)	
Maternal poverty status				
Above federal poverty level	0	4332	51.8 (29.1)	0.0256
	1	247	47.5 (29.4)	
Below federal poverty level	0	1310	43.8 (29.5)	0.0028
	1	87	34.0 (29.0)	

[1]From two-sample, two-tailed t-test comparing mean birth weight percentile among exposed and unexposed gestations

Table 7. Difference in birth weight for gestational age percentile among women exposed to labor market insecurity in first trimester compared to unexposed women by potential effect modifier variables.[1]

Potential effect modifier	Difference in birth weight percentile (95% CI)
Race/ethnicity	
Non-Black/non-Hispanic	-4.63 (-8.51, -0.76)
Black	-4.09 (-8.97, 0.78)
Hispanic	-1.85 (-12.44, 8.74)
Childhood socioeconomic status (father's level of education)	
Low (< 12 years)	-1.55 (-5.93, 2.84)
Average (12 years)	-5.52 (-10.0, -1.04)
High (> 12 years)	-8.66 (-14.04, -3.29)
Educational attainment	
<12 years	-9.20 (-15.76, -2.63)
12 years	-2.55 (-5.88, 0.79)
>12 years	-1.33 (-7.36, 4.71)
Marital status	
Unmarried	-1.85 (-5.32, 1.61)
Married	-5.79 (-10.49, -1.09)
Maternal employment	
Employed	-2.77 (-7.43, 1.90)
Unemployed	6.22 (-4.65, 17.08)
Keeping house	-7.10 (-12.33, -1.87)
Out of the labor force	-10.27 (-18.82, -1.71)
Maternal poverty status	
Above federal poverty level	-3.81 (-7.31, -0.32)
Below federal poverty level	-6.62 (-12.84, -0.40)

[1]Estimates from generalized estimating equations adjusted for maternal age, race/ethnicity, educational attainment, marital status, poverty status, parity, year of birth, and sampling variables.

Table 8. Distribution of exposure to labor market insecurity in first trimester by potential mediator variables and mean (SD) birth weight for gestational age percentile by exposure status within categories of potential mediators

Potential mediator	Labor market insecurity in first trimester (1=exposed, 0=unexposed)	Number (%) in category	Mean (SD) birth weight for gestational age percentile	p-value[1]
Maternal job loss				
Yes	0	409	46.8 (28.2)	0.4952
	1	23	42.7 (29.7)	
No	0	5946	50.1 (29.3)	0.0009
	1	337	44.6 (30.0)	
Household entered poverty				
Yes	0	302	43.8 (29.2)	0.7096
	1	15	40.9 (35.8)	
No	0	3603	50.0 (29.3)	0.0387
	1	257	46.1 (29.5)	
Household income loss				
Yes	0	1438	49.3 (29.1)	0.4939
	1	82	47 (30.9)	
No	0	2201	50.5 (29.2)	0.0451
	1	164	45.7 (29.0)	
Utilization of first trimester prenatal care				
Yes	0	5087	50.5 (29.2)	0.0106
	1	283	45.9 (30.0)	
No	0	1065	47.2 (29.4)	0.0359
	1	66	39.4 (29.1)	
Maternal smoking				
Did not smoke in year of birth	0	4443	53.0 (29.0)	0.0972
	1	233	49.8 (29.0)	
Smoked during year of birth	0	1897	42.4 (28.5)	0.0031
	1	126	34.7 (29.4)	

[1]From two-sample, two-tailed t-test comparing mean birth weight percentile among exposed and unexposed gestations

Table 9. Estimates of total and direct effects of exposure to labor market insecurity in first trimester on birth weight for gestational age percentile and proportion of total effect explained by mediator (PE).[1]

	β (95% CI)	Proportion explained (PE)[4]
Total effect[2]	-4.05 (-6.87, -1.22)	
Direct effects[3] controlling for:		
Maternal job loss	-4.06 (-6.89, -1.23)	0.0033
Household entered poverty	-4.04 (-6.87, -1.21)	0.0022
Household income loss	-4.04 (-6.87, -1.20)	0.0029
First trimester prenatal care	-4.05 (-6.86, -1.25)	0.0014
Maternal net gestational weight gain	-3.61 (-6.29, -0.92)	0.1084
Direct effects by level of potential mediator[5]		
Maternal smoking		
Did not smoke in year of birth	-2.09 (-5.09, 0.91)	NA
Smoked during year of birth	-7.40 (-11.27, -3.52)	NA

[1]Estimates from generalized estimating equations adjusted for maternal age, race/ethnicity, educational attainment, marital status, poverty status, parity, year of birth, and sampling variables.

[2]Total effect = estimate of association for exposure to labor market insecurity in first trimester controlling for potential confounders only

[3]Direct effect = estimate of association for exposure to labor market insecurity in first trimester controlling for potential confounders and potential mediator

[4]PE = proportion of the total effect of exposure to labor market insecurity that is explained by the mediator. PE = total effect minus the direct effect, divided by the total effect

[5]Direct effect = estimate of association for exposure to labor market insecurity in first trimester controlling for potential confounders and potential mediator within levels of mediator (due to statistically significant interaction between exposure and mediator)

Figure 1. Ecological model of birth outcomes.

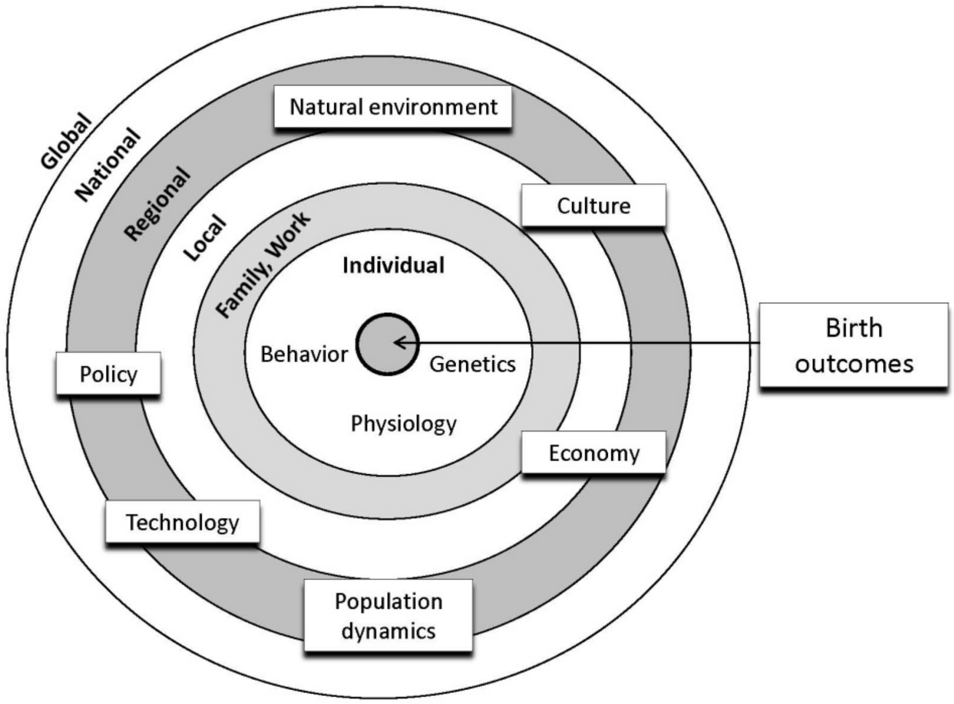


Figure 2. Total number of months (summed over all states) with high labor market insecurity and high labor market security by year, 1980-2009.

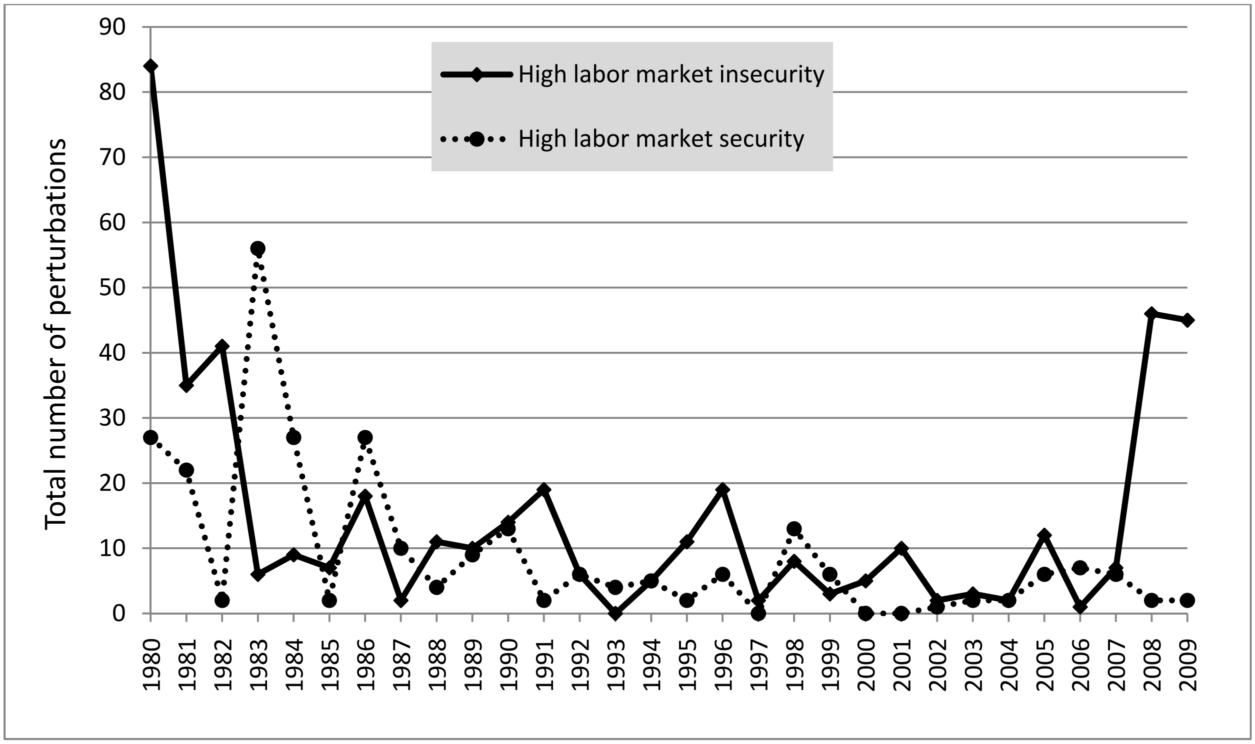


Figure 3a. Box plot of birth weight percentile by labor market insecurity in first, second, and third trimester.

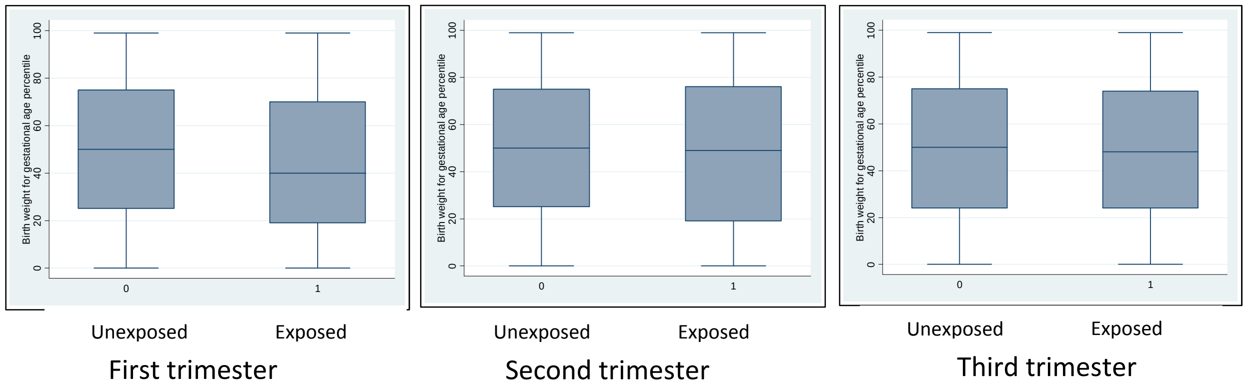


Figure 3b. Box plot of birth weight percentile by labor market security in first, second, and third trimester.

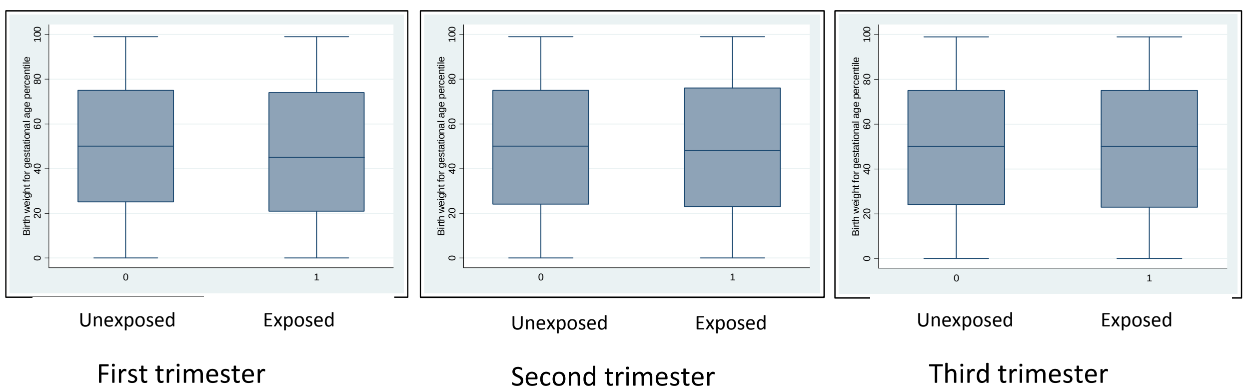


Figure 4a. Percent of gestations in study sample exposed to labor market insecurity during first, second, and third trimester.

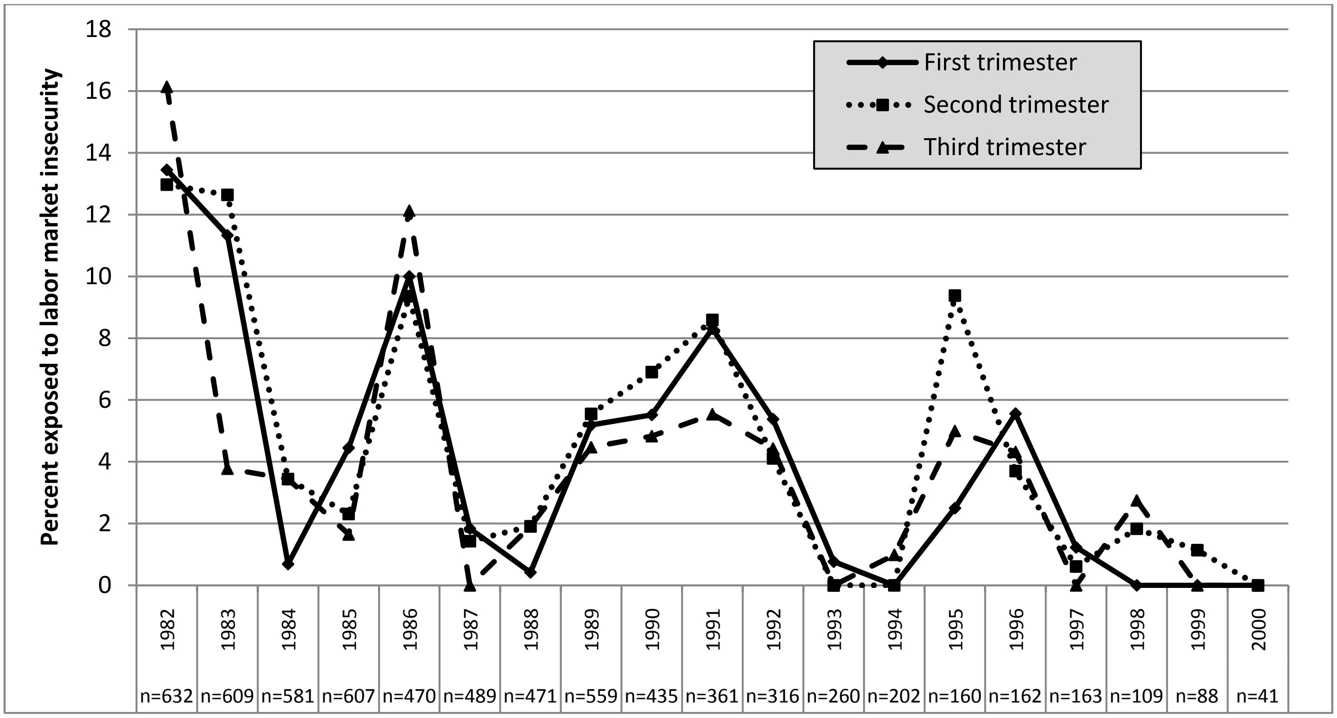


Figure 4b. Percent of gestations in study sample exposed to labor market security during first, second, and third trimester among gestations in study sample (n=6715) from 1982-2000.

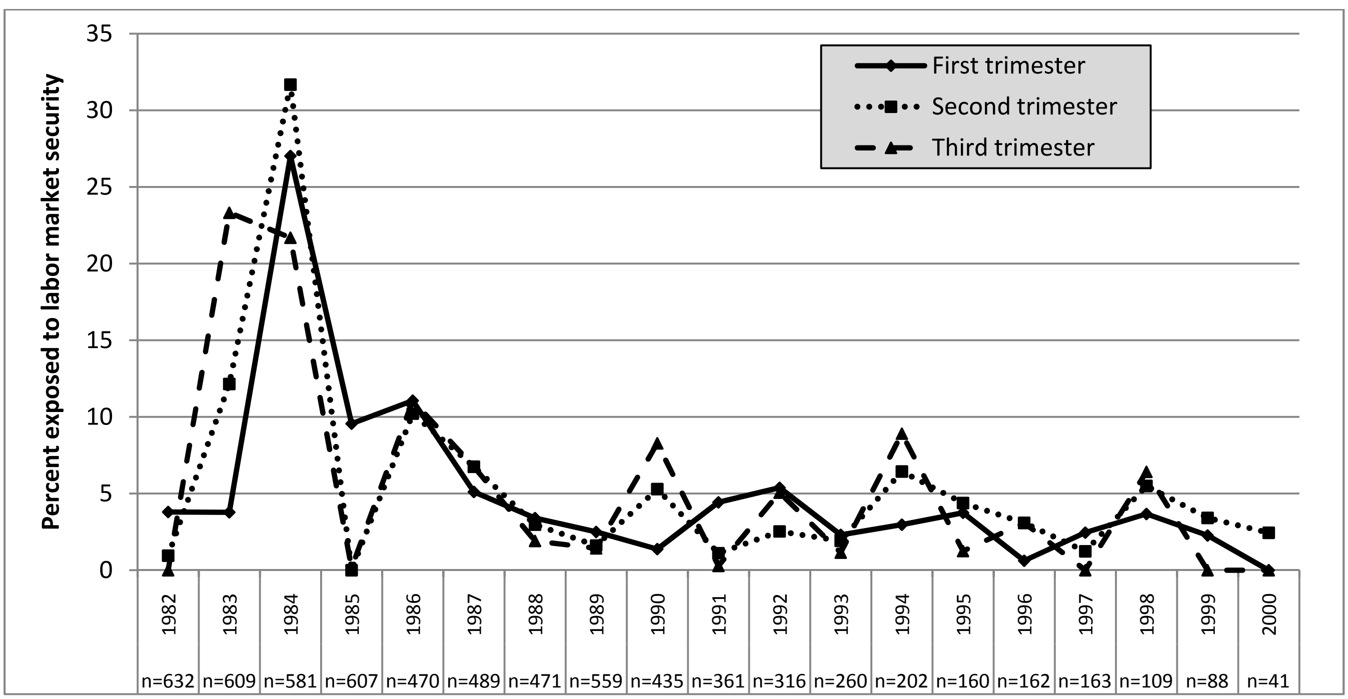


Figure 5a. Mean birth weight for gestational age percentile among gestations in study sample (n=6715) from 1982-2000.

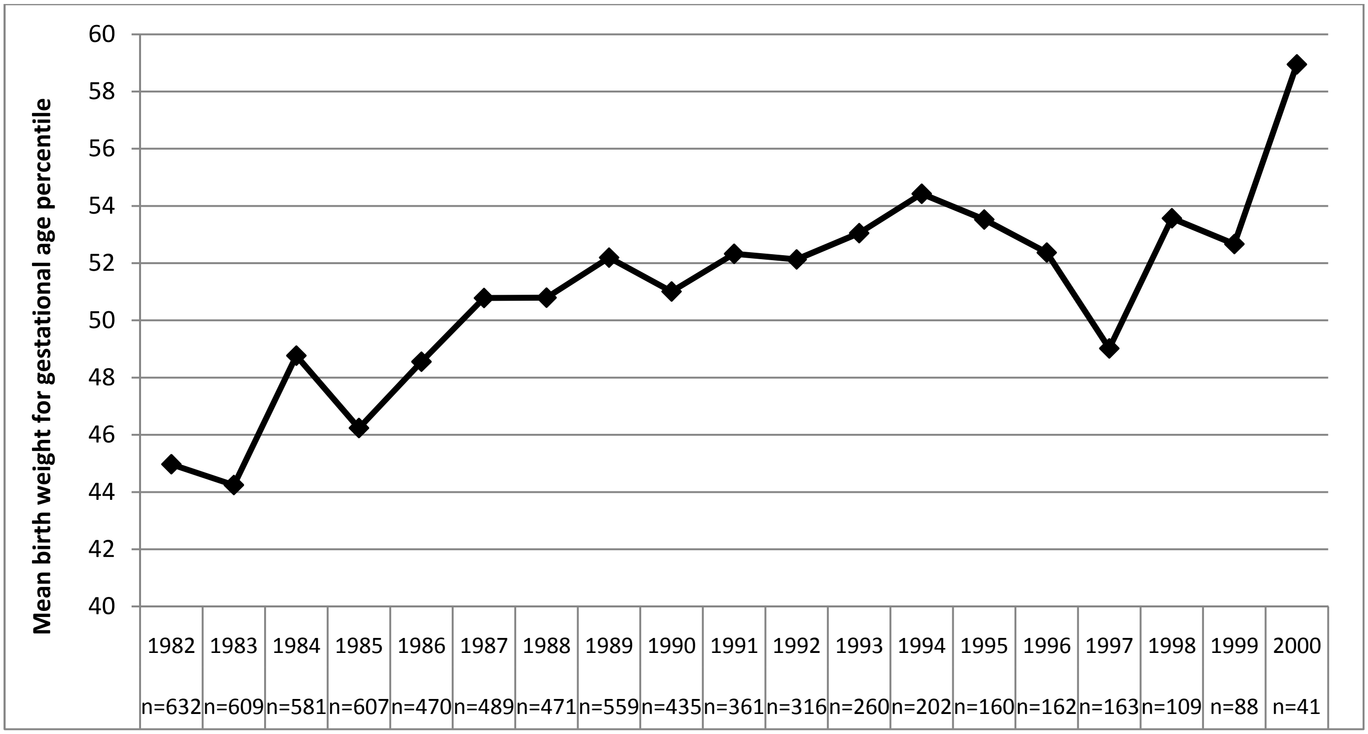


Figure 5b. Percent small for gestational age (SGA) among gestations in study sample.

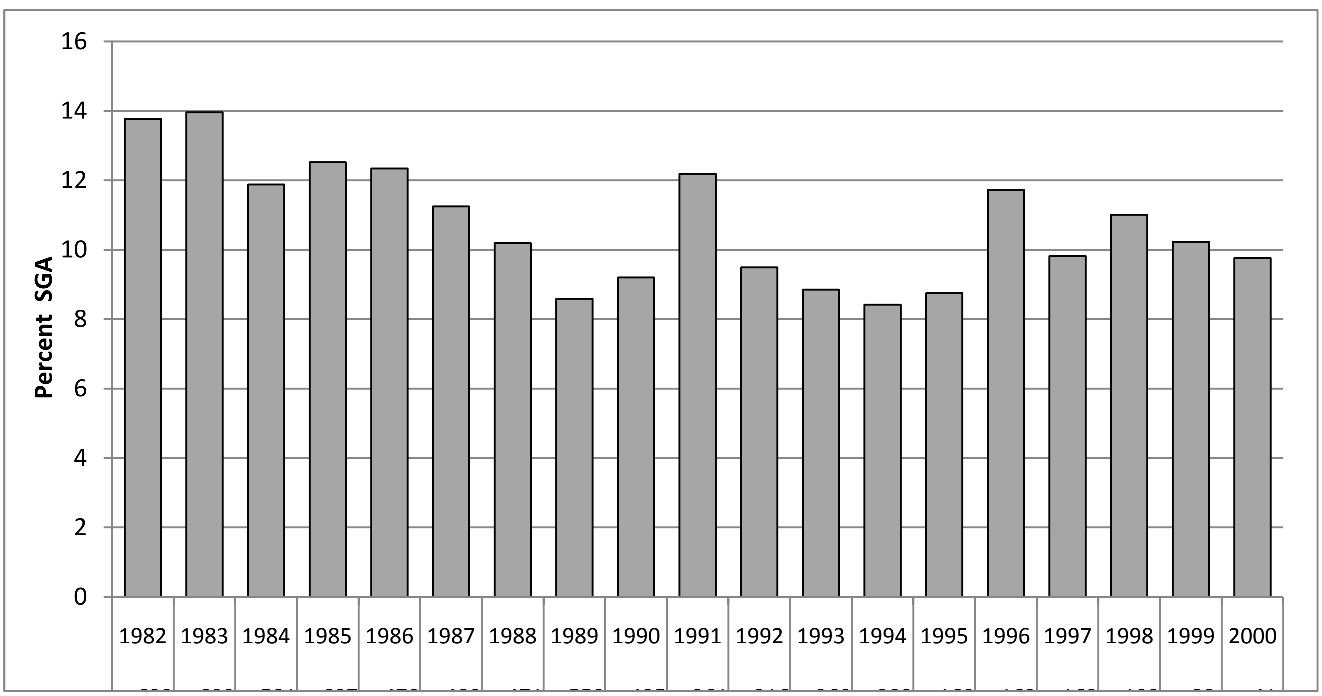
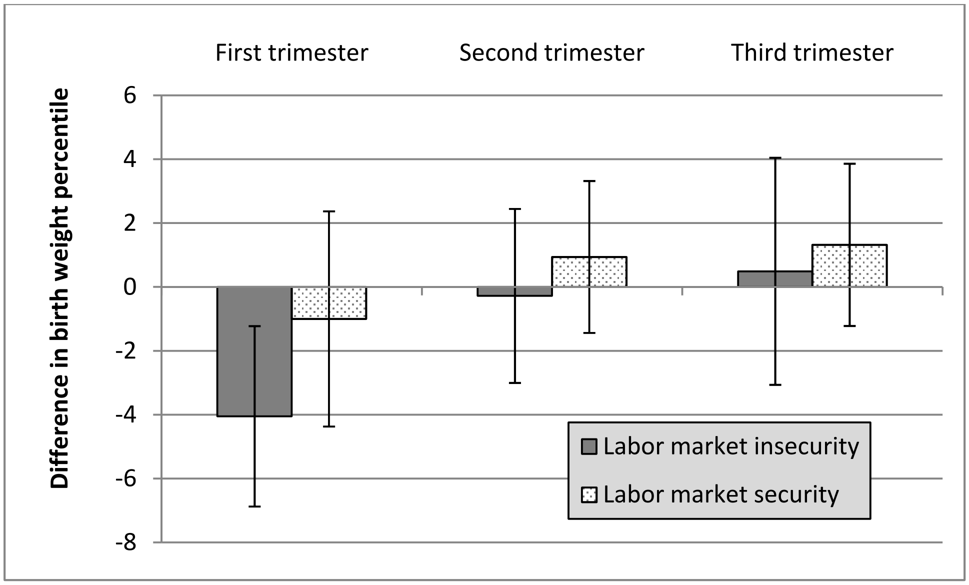
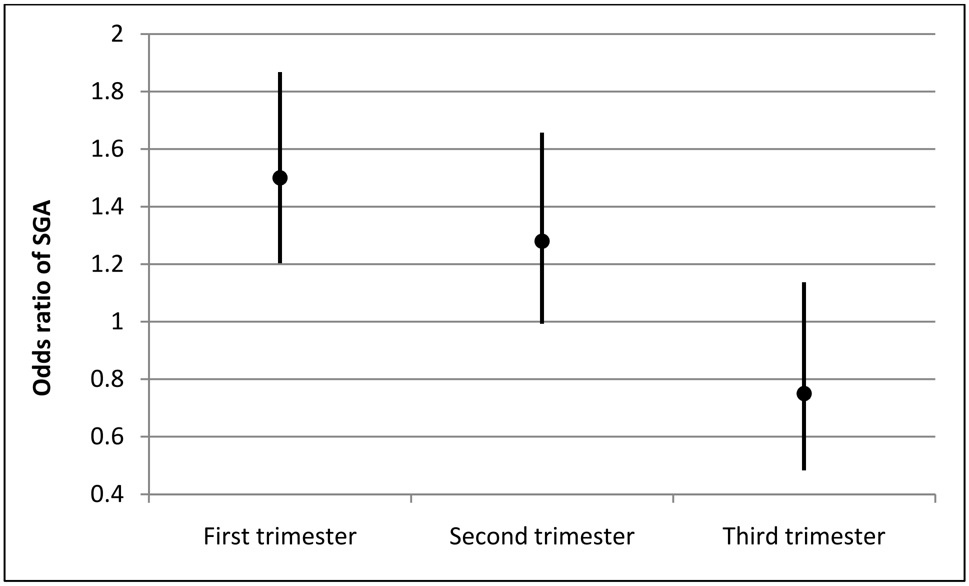


Figure 6. Difference in birth weight percentile among gestations exposed (vs. unexposed) to labor market perturbations during the first, second, and third trimester: results from multivariable models[1]



[1]Estimates from generalized estimating equations adjusted for maternal age, race/ethnicity, educational attainment, marital status, poverty status, parity, year of birth, and sampling variables.

Figure 7. Ratio of odds of SGA among gestations exposed (vs. unexposed) to labor market insecurity during the first, second, and third trimester: results from multivariable models[1]



[1]Estimates from generalized estimating equations adjusted for maternal age, race/ethnicity, educational attainment, marital status, poverty status, parity, year of birth, and sampling variables.

Appendix

Description of variables used in analyses, NLSY79 survey questions from which variables were derived, and units or categorization schemes. For variables that were employed as indicator variables, the reference group is noted.

VARIABLE	SURVEY QUESTION	UNITS/CATEGORIZATION
Exposure and outcome		
Exposure to labor market insecurity during first, second, or third trimester	N/A	For each trimester: Exposed: ≥1 month of trimester classified as having high labor market insecurity (i.e., unemployment rate significantly higher than expected based on time series models)
Exposure to labor market insecurity during first, second, or third trimester	N/A	For each trimester: Exposed: ≥1 month of trimester classified as having high labor market security (i.e., unemployment rate significantly lower than expected based on time series models)
Birth weight for gestational age	Birth weight and gestational age in weeks	Percentile based on national distribution
Small for gestational age (SGA)	Birth weight and gestational age in weeks	Birth weight for gestational age $<10^{th}$ percentile
Covariates (individual maternal characteristics)		
Age		Continuous variable
State of residence	State of residence	Indicator variable for each state
Race/ethnicity	Based on combination of self-report and NLSY assessment	Black Hispanic non-Black/non-Hispanic (reference)
Educational attainment	Highest grade completed	Low: < high school at survey prior to conception Middle (reference): high school at survey prior to conception High: > high school at survey prior to conception
Marital status	Marital status	Married: currently married

		Never married or other (reference): never married, separated, divorced, or widowed
Household poverty	Based on reported household income and number in household	Low: below federal poverty status at survey prior to conception Other (reference): above federal poverty status at survey prior to conception
Parity	Birth order of child	Parous (reference): ≥1 previous child Nulliparous: no previous children
Pre-pregnancy body mass index (BMI)	Pre-pregnancy weight and height	Underweight: BMI <18.5 Normal weight (reference): BMI 18.5-24.9 Overweight: BMI 25.0 – 29.9 Obese: BMI ≥30
General health	Presence of condition limiting ability to work	Condition: presence of limiting condition at survey prior to conception No condition (reference): no presence of limiting condition at survey prior to conception
Potential modifiers		
Childhood SES	Highest grade completed by father	Low: < high school Middle (reference): high school High: > high school
Employment status	Based on question in NLSY79 replicating the *Current Population Survey (CPS)* of American households conducted by the U.S. Census Bureau for the U.S. Department of Labor	Employed (reference): employed, with job not at work, in active forces Unemployed: unemployed Keeping house: keeping house Out of labor force: going to school, unable to work, other
Potential mediators		
Smoking during pregnancy	Mother's reported smoking during 12 months before child's birth	Smoker Non-smoker (reference)
Utilization of prenatal care	Month of first prenatal care visit	Early prenatal care (reference): first visit in 1^{st}-3^{rd} month Late prenatal care: first visit in ≥4^{th}

		month
Net gestational weight gain	[(Pre-pregnancy weight minus pre-delivery weight) minus birth weight]	Kilograms (kg)
Maternal job loss during pregnancy	Based on woman's report of leaving job in last year, whether last day of job fell within estimated gestational period, and reason for leaving job	Job loss during pregnancy: mother left job during estimated gestational period due to "layoff," "fired," "plant closed," "program ended," or "end of temporary or seasonal job" No job loss (reference): did not leave job during gestational period or left for voluntary or family reason
Household entered poverty during last year	Based on report of household income and number in household from survey closest to conception and prior survey	Entered poverty: household below poverty level in year of birth but not prior No income loss (reference): household below poverty level in year of birth and also prior to birth *or* household not below poverty level
Household income loss during last year	Based on report of household income from survey closest to conception and prior survey	Income loss: household income in year of birth < previous year No income loss (reference): household income in year of birth ≥ previous year