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Luke Baertlein 4/21/2014

# Upward or Downward Mobility: Longitudinal residential trajectories and risk for preterm birth

By

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Master of Public Health

Epidemiology

_____

Michael Kramer, PhD

Faculty Thesis Advisor

# Upward or Downward Mobility: Longitudinal residential trajectories and risk for preterm birth

By

Luke Baertlein

Bachelor of Arts

Saint Mary's University

2012

Faculty Thesis Advisor: Michael Kramer, PhD

An abstract of

A thesis submitted to the Faculty of the
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# Abstract

Upward or Downward Mobility: Longitudinal residential trajectories and risk for preterm birth

By Luke Baertlein

**Background:** Many studies have been conducted on the potential effect of neighborhood deprivation on preterm birth and how this effect varies throughout the life-course. Most of these have been cross-sectional. We investigated the preterm birth risk associated with moving to a lower or higher deprivation neighborhood compared to staying in the same neighborhood through a longitudinal study design. We hypothesized that a decrease in deprivation exposure through upward mobility would be associated with reduced preterm birth risk while an increase in deprivation through downward mobility would result in increased risk.
**Methods:** A retrospective cohort was constructed through linking sibling birth records to 170,865 mothers living in the Atlanta area between 1994 and 2007. The residential addresses were geo-coded and linked to Census measures of neighborhood deprivation, creating a partial adult exposure history preceding the second birth. Fixed-effects multi-level regression modeling was performed to draw comparisons between women who shared a neighborhood at the baseline measurement.
**Results:** Moving to a lower deprivation neighborhood was associated with a decrease in preterm birth risk (OR=0.93, 95% confidence interval 0.88, 0.98) while moving to a higher deprivation neighborhood was associated with an increase in preterm birth risk (OR=1.15, 95%CI 1.09, 1.21), controlling for maternal race, education, and age. The magnitudes of the associations depended on maternal age at baseline, the time between baseline and follow-up births, and the preterm status of the baseline birth. Null associations between mobility trajectories and baseline preterm birth were found, providing some evidence that selection factors alone do not account for the association between neighborhood deprivation and preterm birth.
**Conclusions:** Longitudinal measures of residential mobility and consequent changes in deprivation lend support to a causal association between neighborhood deprivation and preterm birth. Residential mobility trajectories are a tool to improve our understanding of neighborhood effects throughout the life-course.

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**Table of Contents**

## Introduction

The social epidemiology of preterm birth and other birth outcomes has received much attention by researchers over the past few decades. This has resulted in clear descriptions of the prevalence of preterm birth within social groups and a variety of attempts to explain the differences between groups. One particular area that has been studied is the often stark differences in preterm birth rates between urban neighborhoods within the same city, with attempts made to identify characteristics of the neighborhood environment that may lead to poor birth outcomes. Neighborhood deprivation has been one of the most prominent neighborhood characteristics studied as a potential cause of these rate differences. This study seeks to further the understanding of how neighborhood deprivation is related to preterm birth. Evidence for a causal association is assessed through a novel approach centered on individual change in neighborhood deprivation exposure through residential mobility. Upward or downward residential mobility results in either increased or decreased deprivation exposure which may subsequently change preterm birth risk relative to women who remain in the baseline neighborhood. It is hypothesized that, within the same baseline neighborhood, those who move to a lower deprivation neighborhood experience a decrease in preterm birth risk compared to 'control' women who remain in the baseline neighborhood. Similarly, those who move to a more deprived neighborhood are expected to show an increase in preterm birth risk relative to non-movers. The change in risk is expected to be proportional to the extent of upward or downward mobility. Before this question is explored further, the motivation for such a study is shown through a brief overview of the public health importance of

preterm birth, the social distribution of preterm birth, and a review of the theory and literature that has led to the framing of the question as such.

The public health importance of preterm birth is significant both in terms of the health of children and the economic burden it presents to healthcare systems across the globe. Children born preterm are at significantly greater risk of many poor health outcomes later in life, including cerebral palsy, mental retardation, and visual and hearing impairments.[1] Furthermore, 2.48 infant deaths per 1,000 live births in the U.S., approximately 35% of all infant deaths, were related to preterm birth in 2004.[2] Economically, the increased cost of hospitalization of newborns and the costs of the health related complications that result from preterm birth amount to an estimated $26 billion yearly expense to the U.S. healthcare system.[1]

With the magnitude of the problem in mind, an understanding of the social epidemiology of preterm birth could lead to population-based interventions to both lessen the overall public health impact of preterm birth and to reduce the excess burden experienced by some social groups. To begin, the social distributions of preterm birth can be described at various levels of social organization. The degree of variance within groups and the rate differences between groups indicates the high sensitivity of this outcome to social conditions. At the national level, the U.S. leads developed nations in preterm birth rate. From 1981 through 2006, the U.S. preterm birth rate rose from 9.5% to 12.8% and has since fallen to 11.7% in 2012. While this trend was mirrored in other developed nations, their rates range between 5 and 9%, consistently lower than U.S. rates.[3]

Looking closer at the U.S. preterm birth rate, it is apparent that the U.S. is hardly homogenous in terms of rates. When broken down by state, the rate varied from a low of 8.7% in Vermont to a high of 17.1% in Mississippi in 2012. The median rate was 11.3% with a variance of 2.7%.[4] There have not been sufficient ecologic studies to provide state-level explanatory factors for these differences.

The lack of homogeneity continues at lower levels of organization with rates varying between U.S. cities and between counties within the same state. One study that examined the very preterm birth (<32 weeks gestation, as opposed to the standard <37 week definition for preterm) rates by race between Metropolitan Statistical Areas (MSAs) within the U.S. found that the variation in rates by MSA differed between white and black women. For white women, the mean rate was 1.23% with a variance of 0.7%, while the rate for black mothers the mean rate was 8.5% with a variance of 4.8%, a strikingly large difference in variance indicating greater heterogeneity in the city-wide rate between cities among black women than among white women.[5] This brings us from the geographic distribution of preterm birth to the racial distribution.

In the U.S. as a whole, the preterm birth rate among non-Hispanic black women was 16.5% in 2012, compared to 10.3% among non-Hispanic white women and 11.6% among Hispanic women. This disparity is documented at least as far back as 1990, when the white preterm birth rate was 8.5% while the black rate was 18.9%. Between 1990 and 2008 the disparity reduced slightly while the overall rate increased.[6] As the overall rate varies by state, so does the disparity between black and white women. In 2010, the ratio of black to white rates ranged from a high of 1.95 to a low of 0.92, with a mean of 1.52.[7]

While the racial disparity in preterm birth rates has been described at many levels of social organization, it has yet to be sufficiently explained. Some of the research has focused on racial segregation, which produces systematic differences in residential environments, as a possible cause of the disparity. Notably, one of the defining articles of the social epidemiology field, published in 1950, sought to explain racial differences in infant mortality rates in New York through residential segregation and the resulting differences in residential environments.[8]

Before further exploring the associations of neighborhood environment and preterm birth, the distribution of preterm birth by socioeconomic status (SES) should be discussed since individual SES is strongly associated with both neighborhood socioeconomic characteristics such as deprivation and with preterm birth. Low SES has been associated with higher risk of preterm birth among all races and through multiple measures of SES including household income, poverty, and education.[9] A likely problem is incomplete measurement of SES by simple measures such as educational level. A consequence of this is residual confounding when attempting to control for SES as a confounder, such as with when attempting to measure the association between race and preterm birth.

Given the heterogeneity of preterm birth rates at lower levels of social organization and between social groups that have been subjected to residential segregation it is reasonable that characteristics of the neighborhood environment could be causally associated with preterm birth. For example, segregation by race and class has led to differences in the average neighborhood environments between racial and class-based groups. These differences in neighborhood environments could be causal factors

responsible for the race and class based disparities in preterm birth rates. Neighborhood deprivation has been studied as one such potentially causal factor. Multiple studies have found that women living in more deprived neighborhoods tend to be at greater risk of preterm birth. However, the separation of the effect of neighborhood deprivation from the effects of individual race and SES is a complex problem for research in this area. This study approaches the issue from a new direction, focusing on women who share a neighborhood environment at baseline but go on to change neighborhoods and deprivation exposures through residential mobility. The effect of a decrease or increase in deprivation is then estimated, controlling for factors related to both mobility and preterm birth. Women who share the same neighborhood at one point are more likely to be similar on unmeasured factors than women who have never shared a neighborhood or deprivation exposure level. To the extent that these unmeasured factors are confounders of the neighborhood deprivation – preterm birth association, this approach provides a less biased estimate of the effect of neighborhood deprivation on preterm birth. In a counterfactual framework, we are assuming the women who do not move represent the outcome that mobile women would have experienced had they remained in the baseline neighborhood. This is a more reasonable assumption than that made in cross-sectional designs: that the outcomes that would have been experienced by women living in neighborhoods of one deprivation level had they lived in another are approximated by women living in different neighborhoods of different deprivation levels.

## Theory and Conceptual Models

The theoretical underpinnings of the examination of change in exposure to neighborhood deprivation and subsequent preterm birth risk are rooted in the ecosocial theory of disease distribution in combination with the traditional host-agent-environment epidemiologic model. The ecosocial theory has been developed over the past two decades in an effort headed by Nancy Krieger. She describes the theory as an "ecologically oriented, integrative, multilevel, and dynamic epidemiologic framework, explicitly linking societal and biophysical determinants of disease distribution and health inequities – over the life-course and across generations in geographic and historical context."[10] Core constructs of the theory include embodiment, or how ecologic contexts, both social and physical aspects, are manifested in individual biology[11], the life-course, particularly how exposure, susceptibility, and resistance throughout the life-course interact to influence health outcomes, and accountability for social inequities.[10, 12] A crude summary of the theory could be made in three central propositions: First, people live within social and material environments and interact with these environments in complex ways, hence the ecologic approach. Second, these environments influence the health of individuals through a variety of processes of embodiment. Third, larger macro-social factors including economic, political, and social forces act to shape these environments as well as the individuals living in the environment.

In the context of the current study, the residential neighborhood environment is the portion of the broader environment under investigation. The change in environments that occurs throughout the life-course is of central concern. Research in this area has

utilized multiple study designs to examine how an individual's residential history, including history of exposure to neighborhood deprivation, is related to preterm birth. These are later reviewed in detail but the current study focuses on exposures throughout only the adult child-bearing years. By examining change in deprivation exposure through concepts of exposure duration and timing, it may be possible to better understand how this environmental characteristic becomes embodied in poor birth outcomes. For example, if risk increases cumulatively with exposure, a decrease in risk following the removal of exposure would not be expected. If only the environment lived in during pregnancy is relevant to preterm birth risk, then a reduction of risk with reduction of exposure would be expected. This study may shed light on how neighborhood deprivation exposure and preterm birth risk are associated, given that this exposure varies throughout the life-course as individuals move into and out of different neighborhoods.

The dominant proposed pathway of embodiment from neighborhood deprivation to preterm birth operates through psycho-social stress mechanisms. This can best be understood in a traditional host-agent-environment epidemiologic framework.[13, 14] In this framework, neighborhood deprivation would be considered a stressor, i.e. an agent. The woman is the host on which the agent acts, and the environment is conceptualized broadly to include a woman's social network and other characteristics of the neighborhood environment that are not stressors. This framework is useful in that it leads to a consideration of characteristics of host, agent, and environment that may be harmful or protective in terms of experienced stress and preterm birth risk. For example, host factors could include elements such as psychological traits that buffer the effect, or lessen the impact, of stressors; while environmental buffers could include availability of social

support, possibly through marital status, or the presence of public parks. The aspects of the host, agent, and environment interact and change throughout the life-course, creating a complex process of embodiment culminating in stress, chronic stress, and the birth outcome of a woman's child. The concept of chronic stress, which has been used throughout the literature, captures some of the idea that stress throughout the life-course must be considered in order to understand the relation between a stressor and birth outcome. A summary of the condition is that over time, frequent stress experiences result in 'wear and tear' on the body, resulting in 'chronic stress,' a condition characterized by increased susceptibility to stressors and chronically heightened physical indicators of stress, including stress hormones, even in the absence of stressors.[15]

While the pathway from neighborhood deprivation to stress seems plausible, and, when exposure to neighborhood deprivation and other stressors throughout the life-course are considered, the relation between the trajectory of neighborhood deprivation exposure throughout the life-course and chronic stress is plausible. What remains to be discussed is the relation between chronic stress and preterm birth. This has been studied in the medical and biological sciences more than it has in epidemiologic studies. The biological mechanisms that produce the association are not yet understood completely. Preterm birth itself is not a homogenous entity. It may be mild, moderate, or severe depending on the gestational age. The most proximal events leading up to preterm birth may be different as well, possibly indicating several types of preterm birth. The role of maternal stress in each of these pathways may be different.[16-18] Stress is also a construct with multiple domains, roughly separated into the acute and chronic categories. All types of stress are defined by "a person-environment interaction in which there is a perceived discrepancy

between environmental demands and the individual's psychological, social, or biological resources."[16]

With this lack of specificity in exposure and outcome definitions, a clear, single mechanism between the two should not be expected. It is likely that stress interacts with the factors in multiple mechanisms of preterm birth in different ways, leading to the activation of one mechanism that triggers a preterm birth.[16] Wadhwa summarizes the biologic preterm birth mechanisms in the following passage: "Clinical and experimental evidence broadly support the concept that preterm birth is determined by multiple genetic and environmental factors that reflect the interactions among one or more of several pathophysiological processes, which may ultimately share common biological pathways leading to uterine contractions, cervical changes and rupture of membranes. These pathways include (a) early or excessive activation of the maternal-placental-fetal neuroendocrine axis; (b) decidual/chorioamniotic/fetal inflammation caused by ascending genitourinary tract or systemic infection; (c) uteroplacental vascular lesions caused by coagulopathy, hypertension, or abruption/decidual hemorrhage; and (d) pathological distension of the uterus, caused by multiple gestation."[16] Stress may be related to each of these pathways. Activation of the maternal-placental-fetal neuroendocrine axis is known to be influenced by corticotrophin-releasing hormone (CRH), a biomarker of stress. Infection and stress may interact through the effects of stress on immune function. Increased perceived stress is associated with increased c-reactive protein (a biomarker of inflammation), an increase of pro-inflammatory cytokines, and a decrease of anti-inflammatory cytokines. [16-18] The role of stress in the other two pathways, through vascular lesions or hemorrhage, or through multiple gestation is not as clearly

understood. Importantly, there are multiple mechanisms from stress to preterm birth and the interaction between factors in these mechanisms and stress in a complex way is likely to influence the likelihood and severity of preterm birth.

Concerning chronic stress, a ‘cumulative pathways model’ has been postulated.[16] This model posits that the bodies processes that maintain allostasis are gradually worn down through repeat exposure to stressors, or risk accumulation, in a weathering process. From this wearing down, HPA and immune-inflammatory regulation is hypothesized to be deregulated resulting in increased susceptibility to the effects of stress and infection during pregnancy on preterm birth. However, stress and its mediators were not measured in this study. They are important here in that they provide biological plausibility for the causal association between neighborhood deprivation and preterm birth and for a life-course exposure history element to be relevant to preterm birth risk through ideas of biologic weathering or gradual wearing down of biologic systems. For example, reduction of risk after movement to a lower deprivation neighborhood may be plausible if the biological effects of weathering are repaired when adverse exposure is removed.

Neighborhood deprivation, as the primary stressor of interest in this study, is a construct that has been developed through neighborhood effects research that captures a variety of socioeconomic factors and can be generally considered a measure of neighborhood socioeconomic status. To be clear, it is considered as a characteristic of the neighborhood, including both social and physical elements, that is not independent from the socioeconomic composition of the neighborhood, but is substantially distinct. Such characteristics have been described in the literature as ‘contextual’ as opposed to

‘compositional.’ This ‘contextual’ conceptualization of neighborhood deprivation is necessary for the consideration that neighborhood deprivation may cause individual preterm birth. If it was only a compositional characteristic, then control for all individual factors would not leave any unexplained variation, and thus no possible effect.[19] That neighborhood deprivation is dependent on the composition of individual socioeconomic statuses is clear when the measurement of neighborhood deprivation is considered. It can be measured through a conglomeration of individual socioeconomic measures of the people residing in the neighborhood, as measured through the U.S. census.[20] Measurements at the neighborhood level do not directly enter into this measurement at all. This is discussed further when the exact method of measurement used in this study is described.

A core problem of neighborhood effects research is the separation of context from composition when the composition could confound the context-outcome association.[19] If neighborhood deprivation is the contextual characteristic, then potentially confounding compositional factors are the characteristics of individuals that become clustered in neighborhoods with one level of deprivation rather than another when these characteristics are also related to preterm birth. If individual poverty causes an individual to live in a deprived neighborhood and is also associated with preterm birth then the estimated effect of deprivation would be biased unless individual poverty is controlled for. However, neighborhood poverty is a potential cause of individual poverty, thus, if measured only at a single time-point then individual poverty is both a possible confounder and mediator of the effect of neighborhood deprivation and reduction of the confounding bias becomes difficult. This study avoids this problem through measurement

of individual socioeconomic characteristics prior to residential mobility, thus prior to the relevant exposure to neighborhood deprivation.

A second difficulty in controlling for individual socioeconomic factors in neighborhood effects research is the degree of segregation in most U.S. cities.[21, 22] The selection of individuals with a given set of socioeconomic characteristics into one neighborhood and not another is so strong that very few individuals with that set of characteristics may live in a neighborhood of another type. This leads to lack of overlap of confounding factors between neighborhoods and inability to control the confounding bias which has been termed ‘structural confounding’ in the literature.[22] By focusing on residential mobility, with both exposed and unexposed subjects living in the same baseline neighborhood, the likelihood of structural confounding was reduced. The social stratification that leads to structural confounding in cross-sectional studies would lead to inadequate numbers of individuals within each covariate strata in some neighborhoods. This study examines the distribution of confounders by exposure levels within each neighborhood and reports adjusted estimates among the full set of neighborhoods and among the set of neighborhoods where there is sufficient numbers of individuals at each covariate strata to allow adjustment.

To summarize, ecosocial theory guides us to the consideration of neighborhood deprivation as an environmental exposure occurring throughout the life-course and affecting preterm birth risk in complex ways that are likely not captured by measurements of only the neighborhood environment lived in during pregnancy. These considerations led this study to ask what effect the change in neighborhood deprivation that sometimes accompanies residential mobility may have on preterm birth risk. The

life-course change in deprivation exposure is summarized in mobility trajectories that can be upward, downward, or flat. If neighborhood deprivation is causally associated with preterm birth, as the literature suggests, then a change in neighborhood deprivation is expected to result in a change in preterm birth risk. Upward mobility, resulting in lessened exposure to deprivation, is expected to be associated with a decrease in risk relative to an unchanging trajectory while downward mobility, which results in increased deprivation exposure, is expected to result in increased relative risk. The impact of mobility may depend on the amount of accumulated exposure prior to the move, the degree of change in deprivation, and the amount of time between a move to a new neighborhood and child-birth. A discussion of the extent to which measuring preterm birth risk within the same woman under multiple neighborhood deprivation conditions contributes to our understanding of the causal association between neighborhood deprivation and preterm birth is included as well. Before discussing the study design and methodology in more detail, the literature related to its various aspects is reviewed.

## Literature Review

While the way that preterm birth risk changes with change in neighborhood deprivation exposure through upward or downward mobility is the central focus of this study, the association between neighborhood deprivation and preterm birth has to first be established. This has been done through many cross-sectional studies over the last two decades. Recently, focus has turned more towards understanding how different levels of neighborhood deprivation throughout the life-course are associated with preterm birth risk and utilizing more complex study designs to understand whether or not the association seen in cross-sectional designs is causal. These studies are examined in greater detail after the cross-sectional evidence is briefly reviewed.

### *Cross-sectional Evidence of an Association between Neighborhood Deprivation and Preterm Birth*

While the neighborhood deprivation construct has been central to many of the studies examining elements of neighborhood socioeconomic status, there have been many different measures used throughout the literature. Similarly, there have been many different statistical methods used to estimate the effect of neighborhood effects on birth outcomes. Furthermore, the measurement of poor birth outcome differs between studies. Some studies examine low birth weight rates while others examine preterm birth rates or continuously measured birth-weight or gestational age. This makes comparisons between and summary over the various studies difficult. As a result, the study-specific results are

reported here and quantitative generalization is cautioned against. Overall, these studies have shown a consistent association between neighborhood deprivation and poor birth outcomes. The magnitudes have generally been small, with odds ratios between 1.1 and 1.6, roughly. Adjustment for individual-level factors usually moves the effect estimate towards the null, which is to be expected given the positive correlation of individual and neighborhood socioeconomic characteristics. A variety of methods have been used to account for correlation of individuals within neighborhoods and to decompose the variation in outcomes to between- and within-neighborhood variation. Measures of deprivation showed greater variation in earlier studies, but have tended towards use of the Neighborhood Deprivation Index in more recent studies. (Table 1)

**Table 1. Summary of identified studies measuring associations between neighborhood socioeconomic characteristics and birth outcomes without longitudinal emphasis**

| Author | Year | Title | Deprivation Measure | Outcome | Design | Results |
|---|---|---|---|---|---|---|
| Roberts [23] | 1997 | Neighborhood Social Environments and the Distribution of Low Birth-Weight in Chicago | Socioeconomic status: %white-collar workers, median family income, median adult education; Economic hardship: %unemployed, %poverty | Low Birthweight | Cross-sectional; Regression analysis controlling for individual-level variables. | Greater neighborhood economic hardship and lower neighborhood socioeconomic status were associated with significantly greater odds of LBW, controlling for individual factors. Odds ratios were 1.19 (95%CI 1.14-1.25) and 1.10 (95%CI 1.03-1.18), respectively. |
| O'Campo [24] | 1997 | Neighborhood Risk Factors for LBW in Baltimore: A Multi-level Analysis | Unemployment rate, average wealth, per capita income | Low Birthweight | Cross-sectional; Two-stage regression analysis, including conditional (Fixed Effects) logistic regression for tract-specific models and macro-level analysis using coefficients from tract-specific models. | Tract median income <$8000 was associated with increased odds of LBW (OR 1.11 (95%CI 1.02-1.22)), controlling for individual age, education, prenatal care, and health insurance. Indirect effects, or statistical interactions, were found between individual factors and unemployment rate, crime rate, and average wealth, but not direct associations between these factors and LBW. |
| Pearl [25] | 2001 | The Relationship of Neighborhood Socioeconomic Characteristics to Birthweight Among 5 Ethnic Groups in California | Neighborhood poverty, unemployment, and educational composition | Birthweight | Cross-sectional; Linear regression analysis controlling for individual-level variables, generalized estimating equations to account for correlation by hospital of birth, no clustering in neighborhoods. | Overall, neighborhood poverty was associated with a 12 gram decrease in birthweight (SE 4), neighborhood unemployment was associated with a 23 gram decrease (SE 11) and low neighborhood education was associated with a 3 gram decrease (SE 3). Decreases in birthweight by all three neighborhood factors were greater for black women than for white. |
| Pickett [26] | 2002 | Neighborhood Socioeconomic Status, Maternal Race and Preterm Delivery: A Case-Control Study | Median household income, male unemployment rate | Preterm Birth | Case-Control; Logistic regression using generalized estimating equations separately at individual-level and at neighborhood-level, then model with significant variables from both single-level models. | High employment rate and low median household income were associated with increased odds of preterm birth. Associations were non-linear and differed by race. |
| Kaufman [27] | 2003 | Modeling Community-level Effects on Preterm Birth | Median value of owner occupied unit, median household income, %Female-headed households with dependents | Preterm Birth | Prospective Cohort; Multi-level analysis using logistic random intercepts models. | Low Median household income associated with PTB (OR 1.69 (95%CI 1.04-2.78) among black women. For white women, no neighborhood level variation in preterm birth prevalence was found, preventing analysis of neighborhood level factors. |

**Table 1 cont. Summary of identified studies measuring associations between neighborhood socioeconomic characteristics and birth outcomes without longitudinal emphasis**

| Author | Year | Title | Deprivation Measure | Outcome | Design | Results |
|---|---|---|---|---|---|---|
| Farley [28] | 2006 | The relationship between the neighborhood environment and adverse birth outcomes | Median household income, prevalence of boarded up houses | Gestational Age | Cross-sectional; Hierarchical linear regression modeling, random intercepts. | A decrease in median household income by $10,000 was associated with a 0.062 week decrease in gestational age (SE 0.012). One additional boarded up house per 1000 houses was associated with a 0.0012 decrease in gestational age (SE 0.0005). |
| Luo [29] | 2006 | Effect of neighborhood income and maternal education on birth outcomes: a population-based study | Neighborhood median income quintile | Preterm Birth | Cross-sectional; Multi-level logistic regression analysis and ordinary logistic regression (effect estimates did not differ between regression types, only ordinary logistic regression ORs reported). | Lowest neighborhood income quintile compared to highest was associated with an increase in preterm birth odds (OR 1.14 (95%CI 1.10-1.17)), adjusted for maternal education, marital status, age, ethnicity, and other non-sociodemographic factors. Significant trend of increasing preterm birth rate with decreasing neighborhood income quintile. |
| Masi [30] | 2007 | Neighborhood economic disadvantage, violent crime, group density, and pregnancy outcomes in a diverse, urban population | Economic disadvantage index | Preterm Birth | Cross-sectional; Multi-level logistic regression modeling with random intercepts. | Results differed by maternal race. Associations of PTB with economic disadvantage were significant for black but not white women (black OR 1.04, white OR 1.01 (95%CIs not reported). ORs represent association with a one unit change in disadvantage on the index scale. |
| O'Campo [31] | 2008 | Neighborhood Deprivation and Preterm Birth among Non-Hispanic Black and White Women in Eight Geographic Areas in the United States | Neighborhood deprivation index quintile | Preterm Birth | Cross-sectional; Multi-level logistic regression with random intercepts. | Associations varied by area. OR comparing high to low deprivation (Q5/Q1), adjusted for maternal age and education, ranged from 0.90 to 2.24 among white women. Among black women, the adjusted OR ranged from 0.88 to 1.40. Magnitude of association was smaller among black women than white in all 8 areas. |
| Janevic [32] | 2010 | Neighborhood deprivation and adverse birth outcomes among diverse ethnic groups | Neighborhood deprivation index quartile | Preterm Birth (<32 weeks, 32-36 weeks) | Cross-sectional; Logistic regression with cluster-robust standard errors. | < 32 weeks: OR comparing high to low deprivation (Q4/Q1), adjusted for maternal education, ethnicity, age and other individual factors, was 1.24 (95%CI 1.13-1.36). Adjusted for only maternal education, OR was 1.79 (95%CI 1.61-1.98). 32-36 weeks: Q4/Q1 fully adjusted OR 1.06 (95%CI 1.01-1.11). Education only adjusted OR 1.27 (95%CI 1.21-1.34). |
| Schempf [33] | 2011 | The Neighborhood Contribution to Black-White Perinatal Disparities: An Example From Two North Carolina Counties, 1999–2001 | Neighborhood deprivation index | Preterm Birth | Cross-sectional; ordinary logistic regression controlling for neighborhood SES, conditional (Fixed Effects and Random Effects) logistic regression | Neighborhood deprivation index accounted for only a small amount of between-neighborhood variation in PTB rate. Associations between deprivation and PTB not shown. (Study objective was to estimate racial disparity controlling for neighborhood deprivation.). |

*Evidence of a Changing Effect of Deprivation throughout the Life-course: Exposure Timing and Duration*

Studies that have attempted to examine how exposure to neighborhood deprivation throughout the life-course is related to preterm birth have taken a number of different approaches. In combination, they provide evidence that deprivation exposure at the time immediately preceding child-birth, as was measured in the cross-sectional studies, is not the only time at which exposure is relevant. It seems that exposures throughout the life-course at all times preceding child-birth are related to preterm birth risk. The change in exposure over time can be conceptualized as individual mobility trajectories. The evidence and details of associations between deprivation mobility trajectories and poor birth outcomes can be categorized into studies of four types.

First, a set of studies have examined the interaction of maternal age and deprivation exposure.[34-39] These provide indirect evidence of an accumulation of risk with increasing duration of exposure. However, they do not provide any suggestion as to what might happen to risk as exposure changes through residential mobility. Second, the duration of exposure has been estimated through comparisons between immigrant and native-born women.[40-43] Studies of this type have attempted to identify how long an immigrant woman has to live in a deprived area before she takes on the same risk as a native-born woman who is assumed to have been exposed throughout her life. This provides indirect evidence of a potential threshold effect of deprivation, suggesting that a woman has to live in a deprived neighborhood for a certain length of time before it begins to affect her preterm birth risk. An implication of this for the current study is that the

expected decrease in preterm birth risk following a move to a lower deprivation area may not be immediate and the woman may have to live in the new environment for a number of years before the previously accumulated risk decreases.

A third type of study has examined neighborhood change in deprivation, rather than individual change in deprivation exposure, in relation to subsequent preterm birth risk, or ecologically, to neighborhood preterm birth rates.[26, 44, 45] These studies could indicate how preterm birth risk could be changed by a decrease in neighborhood deprivation if a number of conditions were met, including individuals with preterm birth risk having lived in the neighborhood prior to the deprivation decrease as well as after the decrease. However, in the studies identified the conditions do not appear to have been entirely met. Nevertheless, they provide evidence of change in preterm birth rates with change in neighborhood deprivation, which is an important ecological evidence of the potential causality of neighborhood deprivation.

The fourth type of studies is that which measured deprivation at multiple time-points for individual women. These can be subdivided into a set of studies that examined life-long deprivation exposure through a measure at a woman's birth and at the birth of her child [46-49] and a second set that have measured deprivation at multiple adult time-points [50, 51]. The first type provides evidence of the importance of deprivation exposure throughout the life-course and suggests that the effect of deprivation in early life can be reduced by upward mobility to less deprived areas prior to child-birth or increased through life-long downward mobility. Our study seeks to replicate this design, but on a much shorter time scale, focusing on mobility between child-births. The second type has provided evidence of accumulation of risk with cumulative adult exposure to

deprivation. This suggests that woman moving to lower deprivation areas may not be experiencing a decrease in risk, rather, those who continue to live in a high deprivation area may be experiencing an increase in deprivation. This study may be able to roughly distinguish between these two scenarios by measuring the risk difference for preterm birth risk at first birth and risk at second birth and comparing the risk difference between those women who move and those who stay, with shared neighborhood at baseline.

*Duration of Exposure Approximated by Maternal Age*

Following the weathering hypothesis, there has been a number of studies conducted to examine the change in the association between deprivation and preterm birth with maternal age. The weathering hypothesis was initially proposed in1996 as a mechanism to account for the greater rate of increase in poor birth outcome risk with age among black compared to white people.[34] The hypothesis is that increased exposure to chronic stress among blacks leads to a left-ward shift in the curve of poor birth outcome-risk with age. The result being that the risk experienced by blacks starts to increase at younger ages and increases at a greater rate than that experienced by whites. The theory does not require a racial component and has been expanded to consider low socioeconomic status and other potential chronic sources of stress. In the context of neighborhood deprivation, the hypothesis is that risk for preterm birth accumulates with age such that, among women exposed to neighborhood deprivation throughout their life, the risk of preterm birth increases with age at a greater rate than women never exposed to neighborhood deprivation. In statistical language, there is a hypothesized positive

interaction between age and neighborhood deprivation exposure on preterm birth that may be non-linear and possibly quadratic.

This hypothesis has been investigated by at least six studies, including the study in which it was initially proposed by Geronimus. This first study found that the association between area income and LBW increased as age increased. The primary focus of the study was on the interaction of race and age on the association with poor birth outcome. However, it was found that among black women living in high income areas the increase in LBW risk with age did not differ from that of white women. This suggests a possible three-way interaction between race, neighborhood deprivation, and age on poor birth outcome risk. [34] A later study found further evidence of the age and neighborhood poverty interaction among black but not white mothers on the risk of LBW.[35] Further evidence of an interaction of maternal age with neighborhood deprivation was found in a study using multi-level regression analysis to assess how the association between age and birthweight varied between neighborhoods. Neighborhood poverty accounted for 44% of the between-neighborhood variation in the association of age and birthweight.[36] The dependence of the association of age and birth outcome on experience of neighborhood poverty was tested by a study that utilized the Illinois Trans-generational Birth File to classify women as experiencing life-long exposure to poverty and life-long exposure to high SES neighborhoods. While the ‘weathering’ effect, or the increase in low birthweight risk with increasing age, was found among those exposed to life-long poverty, the risk of low birthweight was found to slightly decrease with age among women exposed to life-long high SES neighborhoods.[38]

This area of research provides strong evidence that the association between neighborhood deprivation and birth outcomes is not static throughout the life-course. The cross-sectional design of these studies is a limitation as it does not allow for exposure duration to be explicitly measured. Age appeared to be conceptualized as a proxy for exposure duration. The tenability of this assumption depends on the extent of residential mobility in the cohort. However, if the assumption holds, then the increase in risk with increase in exposure duration provides some evidence for an accumulation of risk model of the association between neighborhood deprivation and poor birth outcomes. However, this design cannot distinguish between this scenario and one in which susceptibility to neighborhood conditions increases with age. A more explicit measure of exposure duration, allowing statistical control for maternal age and taking residential mobility into account, would be necessary to distinguish these two possibilities.

*Duration of Exposure: Studies of Immigrants*

A seemingly unlikely avenue toward approximating exposure duration can be found in a body of literature comparing the association between neighborhood deprivation and poor birth outcomes between immigrant and native-born women. It is hypothesized that foreign-born women have shorter duration of exposure to the neighborhood environment immediately preceding child-birth than native-born women and consequently have lower risk of poor birth outcomes. Again, this explanation assumes residential stability, aside from that resulting from immigration.

The primary support for this theory comes from a series of studies conducted in Canadian populations.[40-42] The first compared recent immigrants to longer-term immigrants and found that the risk ratios estimating the association between neighborhood median income and preterm birth were greater for longer-term residents than for recent immigrants (RRs 1.34 and 1.03, respectively, adjusted for maternal age).[40] These findings were expanded upon in the second study which measured time since immigration for foreign-born women immigrating within five years prior to child-birth. In this cohort, no association between neighborhood SES and low birth-weight was detected.[41] The cohort was then expanded to included women with up to 22 years since immigration. The expected association between neighborhood deprivation and low birth-weight was found only among women with 14 or more years since immigration.[42] This indicates the possible utility of a threshold model of exposure duration. It could also support the accumulation model since the smaller effects coinciding with less exposure duration would be harder to detect. Given the sample size of the cohort, it could take 14 years of accumulation for the effect to become visible.

A similar study design was replicated in a U.S. cohort in which native-born and foreign-born black women were compared.[43] While preterm birth rates were higher in higher deprivation neighborhoods, there was no significant difference in the neighborhood-specific preterm birth rates between foreign born and U.S. born women. This is in contradiction to the hypothesis that neighborhood deprivation exposure duration, as approximated by country of origin, alters the effect of neighborhood deprivation on preterm birth risk.

The limited number of studies in this area and the limitations in the design as an unintended method of assessing exposure duration suggest that caution should be taken in placing weight on the evidence from this area for showing how the effect of neighborhood deprivation on birth outcome changes throughout the life-course or for providing evidence of a causal association between neighborhood deprivation and poor birth outcome. A primary limitation is that neighborhood deprivation prior to immigration was not assessed; undermining the assumption that time of immigration can be used to assess exposure duration. Also, there may be other elements aside from exposure duration that correspond with time since immigration, such as acculturation, that gradually increase susceptibility to neighborhood deprivation. Nevertheless, the studies by Urquia [40-42] do seem to suggest that the effect of neighborhood deprivation on poor birth outcomes may vary depending on a woman's life-history, e.g. her immigration status.

*Studies of Life-long Deprivation Trajectories*

A more complete mobility trajectory has been constructed through a third type of study design that utilized inter-generationally linked birth records, linking a woman's own birth record to that of her child. The neighborhood deprivation at each record then forms a two-time point residential history for the woman. If each point is in a high deprivation area, the woman is conceptualized as having life-long exposure to high deprivation, for example. Women who are born into high deprivation but have their children in low deprivation areas are conceptualized as experiencing upward mobility.

The first study of this type used a measure of household poverty rather than neighborhood deprivation, but found that low birth-weight rates were lower among upwardly mobile women than among chronically poor.[46] The other three, all conducted using the Illinois Trans-generational Birth File, assessed neighborhood poverty or deprivation and found similar results.[47-49]

The series of studies found that among black women with high neighborhood poverty at birth, those who remained in high neighborhood poverty at child-birth had a low birth-weight rate of 16% while those who experienced some upward mobility had a rate of 12% and those experiencing high upward mobility had a rate of 10%. The reverse trajectories showed the same pattern: those with low deprivation at birth who remained in low deprivation at child-birth had a rate of 9% while those who had some downward mobility had a rate of 10% and those with a high downward mobility had a rate of 12%.[47] The comparison of those born into the high poverty areas but moved to a lower poverty to those born into the low poverty who remained in low poverty shows similar low birth-weight rates (10% and 9%, respectively), leaving some ambiguity as to whether the initial poverty alters the effect of later poverty exposure or if the exposure at child-birth or during pregnancy is the only significant exposure. When neighborhoods were categorized by median income quartile and restricted to women born into the lowest income neighborhoods, a similar trend in normal weight preterm birth rates was found comparing different degrees of upward trajectories to women with life-long residence in the lowest income neighborhoods. For a one quartile increase, the risk ratio (RR) compared to staying in the low income areas was 0.8. For a two quartile increase, the RR was also 0.8 and for a three quartile increase the RR was 0.6. This suggests that moving

to a lower deprivation area can alleviate the effect of past exposure to high deprivation and provides some evidence for a dose-response relationship.[48]

Place characteristics were further specified beyond neighborhood deprivation to classify neighborhoods within an MSA as urban, suburban or outer region in the most recent study.[49] Restricting the cohort to women born in urban neighborhoods, those who moved to the suburbs had reduced preterm birth risk compared to those who stayed in urban neighborhoods. This transition may be another measurable domain of upward socioeconomic mobility through residential mobility. However, the separation of effects of individual socioeconomic mobility are difficult to separate from the effects of place in this study design without much more complete measures of individual SES.

*Gentrification as a Change in Exposure without Residential Mobility*

While the previous review of studies had focused on residential mobility to estimate neighborhood deprivation exposure history, there have been at least two studies that have examined change in neighborhood deprivation through neighborhood change rather than through change of neighborhood, i.e. through gentrification rather than residential mobility. The first study was ecologic in design, assessing the association between change in neighborhood low birth-weight rates and change in neighborhood employment and educational composition. However, no association was found.[44] The second was multi-level in design, assessing individual preterm birth risk in association with neighborhood gentrification.[45] Black women living in high gentrification areas were found to have increased risk of preterm birth while white women living in these

areas had reduced risk. However, duration of residence in the neighborhood was not measured, so it is unknown if the individuals were exposed to the pre-gentrification neighborhood conditions. The interaction between race and gentrification could be explained by black women living in newly gentrified areas being more likely to have lived in the area prior to gentrification than white women. If a study of gentrification and birth outcomes were to measure duration of residence in the neighborhood, it may provide a way to assess change in neighborhood deprivation exposure that is less confounded by change in individual SES than studies focusing on individual residential mobility. However, all residents of a neighborhood would be exposed to the same change in deprivation exposure, making causal associations reliant on comparisons of different neighborhoods, those that underwent gentrification and those that did not, which may differ on many compositional and contextual factors that could confound the association.

*Studies of Adult Deprivation Trajectories*

A final way in which how the effect of neighborhood deprivation changes throughout a woman's life-course has been through a more complete measure of exposure history during the child-bearing years of adult life. This was done in a way similar to the inter-generational studies mentioned previously, but rather than linking birth records of mother and child, this method linked the records of siblings, creating neighborhood measures for the mother at each child-birth. Two studies of this type have been conducted.[50, 51] The first focused on public housing and transitions to private or mixed-income housing rather than neighborhood deprivation and found minor changes in

preterm birth risk associated with specific transition patterns. The second more directly assessed neighborhood deprivation across multiple births and provides a great deal of information as to how exposure history is related to poor birth outcome.

This study calculated cumulative adult exposure to neighborhood deprivation through linking siblings' geo-coded birth records together to form partial residential histories for mothers. The neighborhood deprivation at each birth was then averaged and multiplied by the number of years between the births. This creates a measure of deprivation-years that can be summed to estimate cumulative exposure to neighborhood deprivation. Among women with high deprivation at first birth, a trend of increasing cumulative neighborhood deprivation with age was found, with generally slightly greater accumulation among black women compared to white. Among women with low or average neighborhood deprivation at first birth a trend of decreasing cumulative deprivation with maternal age was found, with a greater rate of decrease with age among white women, compared to black. The association between cumulative exposure and preterm birth was found to depend on prior preterm birth. Women with a prior child born preterm had a greater rate of increase in risk with increase in cumulative deprivation than women without a prior preterm birth. There was also an interaction between maternal age and cumulative deprivation. Among Black women, the magnitude of the association between cumulative deprivation and preterm birth risk increased with age and, among those with low cumulative deprivation, age was not strongly associated with preterm birth risk. Among white women, high cumulative deprivation was associated with increased risk of preterm/low birthweight, but the magnitude of the association did not appear to change significantly with increasing maternal age.

The primary impact of the results of this study on the understanding of how life-course deprivation exposure history may be related to preterm birth risk is in its finding that the effect of exposure at the time of child-birth or during pregnancy is not independent from prior adult exposures. This had not been previously assessed through multiple measurements of deprivation exposure. Furthermore, this study provides some support for an accumulation of risk model. Our study of residential mobility trajectories could provide information as to whether this risk can be reduced by moving to lower deprivation areas. A challenge this poses to our study of residential mobility trajectories is its ability to distinguish between a reduction in risk following a decrease in exposure level and a lack of further accumulation of risk. Comparing a woman who moves to a lower deprivation area to a woman who stays at the same level of deprivation can have two interpretations if the accumulation of risk model is accurate. The risk of the staying woman can increase while the risk of the moving woman remains constant or the risk of the moving woman can decrease while the risk of the staying woman can remain the same. A combination of these two processes could also occur, with upwardly mobile women decreasing in absolute risk while non-mobile women increase in risk. Reliance on the relative risk between the two does not allow these processes to be distinguished.

*Summary*

A life-course perspective encourages the examination of individual mobility trajectories through residential histories instead of focusing solely on the exposure to neighborhood deprivation immediately prior to child-birth or any other single time-point

in relation to preterm birth. Studies have approached this challenge from a variety of angles. The earlier studies relied on single time-point measures of deprivation but focused on the interaction between maternal age and deprivation as a rough approximation of exposure duration. These studies were largely consistent in their findings that the risk associated with living in a deprived neighborhood increases with age. Due to the over-representation of black women in deprived neighborhoods, this explained a portion of the differential increase in risk with age among black women compared to white. A series of studies examining the association between neighborhood deprivation and preterm birth among foreign-born women found that the exposure to neighborhood deprivation immediately preceding child-birth did not have an effect unless the woman had immigrated at least 14 years previously, implying that a woman has to live in a deprived area for a minimum number of years before the deprivation exposure has an impact on preterm birth risk.

Following these findings, studies with longitudinal designs began to appear, with at least two actual measurements of exposure to deprivation at different points in the life-course. The first type of these measured deprivation at birth and at child-birth, conceptualizing these as life-long mobility trajectories. The association between deprivation at child-birth and poor birth outcome was found to depend on the mother's deprivation exposure at birth. Upward mobility was found to decrease the effect of early-life exposure relative to staying in high deprivation areas. While this shows that exposure histories are an important area to study, the measurements were so far apart that there could likely be a variety of types of mobility trajectories among the rough categories

formed by two distant time points and individual SES likely changed substantially as well.

By focusing on change in exposure during adult years, the impact of specific trajectories on poor birth outcomes can be better identified. Studies did this by looking at change in deprivation exposure through neighborhood gentrification and through multiple adult measures of deprivation, taking residential mobility into account. The study of gentrification was inconclusive in its implications for deprivation trajectories in relation to preterm birth because gentrification involves significant residential mobility into and out of the gentrifying neighborhood and the study relied on single time-point measures of neighborhood, leaving it uncertain which women were exposed to both prior and post gentrification deprivation conditions and which were only exposed to the post-gentrification neighborhood. The study of cumulative adult exposure had specific findings that are difficult to interpret in terms of mobility trajectories due to interactions with race, age, and prior preterm birth. However, that among women with the same exposure at child-birth, those with greater cumulative exposure were at greater risk than those with less cumulative exposure provides some support for an accumulation of risk model. Taking the accumulation model into account, the model below (Figure 1) presents the expected associations, ignoring confounding variables for simplicity, between upward and downward mobility trajectories and preterm birth.

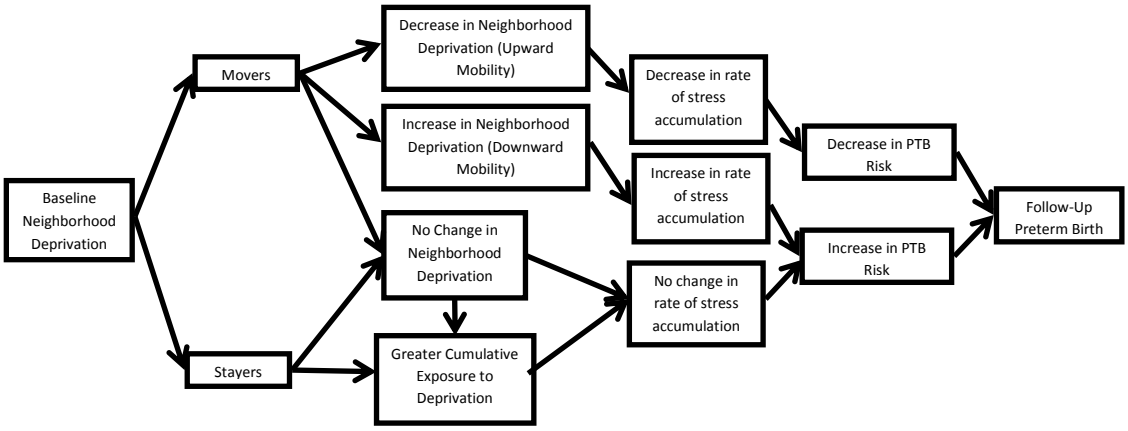


Figure 1. Conceptual diagram of the association between neighborhood deprivation exposure trajectories, stress accumulation, and preterm birth.

As a whole, these studies suggest that examination of specific adult mobility trajectories may improve our understanding of how exposure to deprivation throughout the life-course is associated with poor birth outcomes. Furthermore, by assessing residential mobility as a means to change deprivation exposure, the possible efficacy of interventions aimed at reducing deprivation exposure among high-risk women through aid in upward mobility or prevention of downward mobility can be partially assessed.

*Study Objectives and Research Questions*

The objective of this study is to assess the role of residential mobility and deprivation mobility trajectories in the association of neighborhood deprivation with preterm birth. If exposure to neighborhood deprivation prior to child-birth is a cause of preterm birth, then women who move to lower deprivation areas are expected to experience a decrease in risk compared to women who stay in the same neighborhood. Likewise, those who move to a higher deprivation area are expected to experience an increase in risk. This study quantifies the magnitude of this increase and decrease.

Furthermore, a larger magnitude of increase or decrease in exposure is expected to be accompanied by a larger change in preterm birth risk following a dose-response relationship. This trend is partially assessed.

The primary research question we attempt to answer is: Among women sharing a baseline neighborhood, do those who move to a lower or higher deprivation neighborhood experience a change in preterm birth risk relative to those who stay in the same neighborhood? This contains several components that will be addressed. First, is there an association between upward or downward mobility and subsequent preterm birth? Second, is this association due solely to individual differences between the upwardly or downwardly mobile and the non-mobile or is there evidence of a causal process taking place between baseline and follow-up which results in a change in risk? If there is evidence that risk is changing between time-points, is there also evidence that this change depends on the direction and magnitude of mobility? Finally, does the magnitude of the change in risk associated with change in deprivation depend on the duration of time lived in the new neighborhood, the timing of the mobility in an individual's life-course, or the individuals baseline deprivation exposure?

## Methods

*Study Design*

A population-based cohort of women with two or more child births between 1994 and 2007 in the Atlanta area was constructed through linkage of siblings' birth records to mothers and geocoding the residential address on each record. This created a longitudinal residential history for each woman with a baseline birth and follow-up birth. The exposures considered are neighborhood deprivation trajectories, defined by the change of neighborhood and change in neighborhood deprivation from baseline to follow-up births. The associations of upward and downward mobility with the follow-up birth being preterm were assessed through comparisons to women who did not change neighborhoods between births.

*Causal Diagrams*

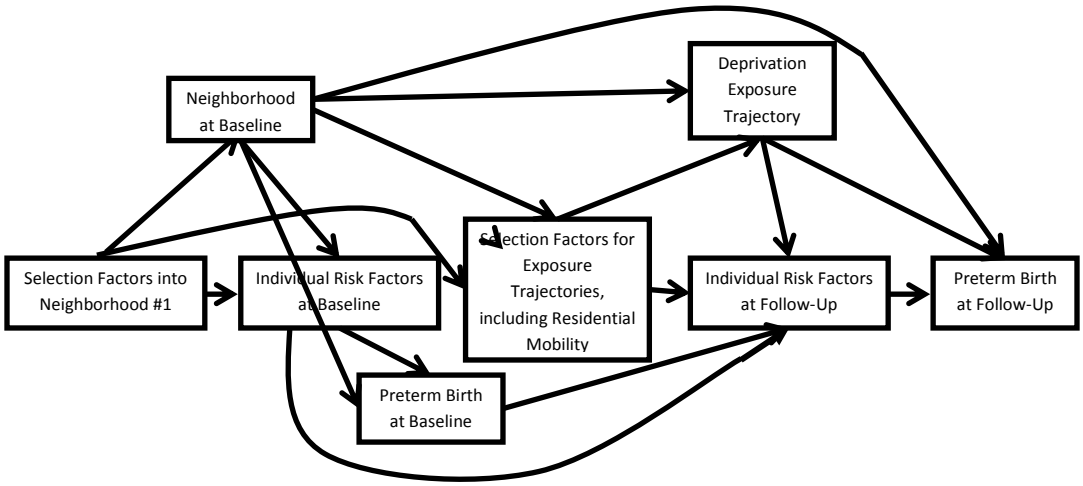


Figure 2. Conceptual Directed Acyclic Graph (DAG) showing the association between deprivation exposure trajectory and follow-up birth preterm. Not all of these variable sets were measured. If measurements of all variables were available, control for neighborhood at 1st record and selection factors for exposure trajectories would be sufficient to isolate the direct and indirect effects of deprivation exposure trajectories.

The goal of this study is to assess the association between exposure to change in neighborhood deprivation and preterm birth at the follow-up birth. The total, direct, and indirect effects could be estimated if the neighborhood at baseline, selection factors for deprivation mobility trajectories, and individual risk factors at follow-up could all be measured completely and appropriately controlled for. Unfortunately, this is not possible given the structure of the data. The data comes from the birth records which does not enable us to distinguish between individual risk factors and selection factors, since these were both measured at the same time-point: at the point of the respective birth. The measures available are presented in the diagram below. Note that this is an improper DAG because the direction of causation is possibly in both directions for some associations.

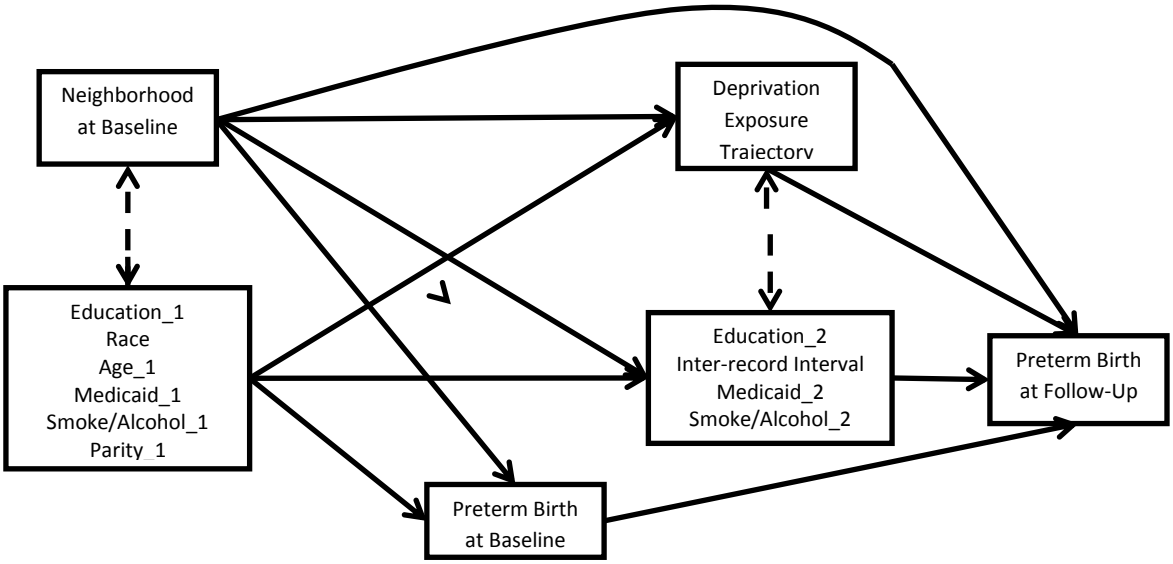


Figure 3. DAG with available measurements. Control for baseline predictors of exposure, neighborhood at baseline, and preterm birth at baseline controls for confounding, provided the individual factors at level 2 are mediators and not confounders. Additional control for these follow-up factors may provide a less biased estimate of the total effect or an estimate of the direct effect, depending on the direction of causality between exposure trajectory and these factors.

To control for confounding completely in this structure, neighborhood at baseline and the individual factors at baseline would have to be controlled. This is accomplished

through matching women on baseline neighborhood in design and controlling for the individual factors at baseline in analysis. Because the individual risk factors for preterm birth at baseline are likely incompletely measured, particularly individual SES, control for baseline preterm birth may be appropriate to control for some of this unmeasured confounding.

*Measures*

*Outcome: Preterm Birth*

Preterm birth was defined as a live birth prior to 37 completed weeks of gestation. The gestational age was reported on the birth record and measured by a possible variety of techniques that may have varied between women. While there has been much discussion of how to ensure accurate and precise gestational age measurement, [52-56] the impact of different estimation techniques would not be expected to be associated with the deprivation mobility trajectories and therefore not confound the results.

*Exposure: Neighborhood Deprivation Mobility trajectory*

Neighborhood deprivation was estimated using the Neighborhood Deprivation Index, developed by Messer et al. in 2006.[20] Neighborhood-level socioeconomic variables prior to the development of the index were often conceptualized as markers of underlying neighborhood deprivation and were highly correlated within studies (see Literature Review Table 1). By aggregating these variables into a general index, the

measure becomes less susceptible to minor variations in individual socioeconomic variables. For example, the median income of two neighborhoods that are identical on poverty rate, educational composition, and unemployment rate may differ without the underlying deprivation of the two neighborhoods differing. If median income alone was used to estimate deprivation, a false distinction between the deprivation levels in these two neighborhoods would be measured. However, if the index is used, combining many of these variables into one measure, then it is more likely that the two neighborhoods would be classified as having similar deprivation levels. The index also facilitates comparisons between different studies and different populations.

The neighborhood deprivation index was developed from a group of 20 census variables that had been identified in the literature as factors approximating neighborhood deprivation. Principal components analysis and factor analysis were used to reduce the number of variables to eight and to weight these appropriately to create a standardized index. The variables in the final index are percent of males in management and professional occupations, percent of crowded housing, percent of households in poverty, percent of female headed households with dependents, percent of households on public assistance and households earning less than $30,000 per year, percent with less than a high school education, and percent unemployed. These represent five domains of neighborhood disadvantage: poverty, occupation, housing, employment, and education. Since the creation of this measure, it has been used successfully by many subsequent studies.[31-33] Messer's article reporting the development of the index is cited by 41 articles in PubMed at the time of this writing, indicating the extent to which the index has been used.

Neighborhood boundaries were approximated by Census tract boundaries based on the geography of the 2000 U.S. Census. The 10-county study region was divided into 564 non-overlapping tracts, or neighborhoods. The neighborhood at the each record was measured through geo-coding the residential address from the record. The dataset was limited to women whose address could be geo-coded at the street-level, leading to less misclassification of neighborhood.

The measures of neighborhood deprivation were created for prior studies that included the entire state of Georgia and used the Neighborhood Deprivation Index to estimate deprivation.[51] The technique is briefly reported here and can be found in more detail elsewhere.[51] Census measured variables aggregated to the tract level were collected from the 1990 and 2000 decennial census and from the 2005-2009 American Community Survey. Neighborhood deprivation was measured in each of these datasets through the Neighborhood Deprivation Index. Linear interpolation of these three points for each tract was used to create a year-specific estimate of neighborhood deprivation for each tract for each year 1994-2007. These values were then normalized so that a value of zero represented the state-wide average deprivation score in 2000 while a value of +1 or -1 represented a 1 standard deviation higher or lower deprivation, respectively, based on the distribution in the full state-wide cohort. A separate index specific to the 10-county region was not calculated as it would not be necessary given our intention to categorize based on deprivation quintiles.

Baseline deprivation was measured using the birth-year and neighborhood specific Neighborhood Deprivation Index for the year of each woman's first eligible recorded birth in the study time period. This allows some variation in baseline

deprivation within neighborhoods but the variation between neighborhoods is much larger. It also allows for the assessment of neighborhood change over time to evaluate the assumption that those who do not move between births do not substantially change deprivation exposures. To increase the simplicity and interpretability of results, baseline neighborhood deprivation was divided into quintiles based on the full distribution of continuously measured baseline deprivation values. The most deprived neighborhoods are in the $5^{th}$ quintile while the least deprived are in the $1^{st}$.

Deprivation mobility trajectories were defined by a combination of residential mobility and change in neighborhood deprivation between first and second birth records. Residential mobility was measured as a binary variable indicating whether a woman changed census tracts between births. Women who's residential census tracts were not equivalent between subsequent births were defined as 'movers' while those whose tracts were equivalent were defined as 'stayers.' The change in deprivation among movers was measured by the difference between the continuously measured deprivation at the $2^{nd}$ record and deprivation at the $1^{st}$ record. A negative value for the change in deprivation represents a decrease in deprivation, or upward mobility, while a positive value represents an increase in deprivation, or downward mobility. Similarly, the change in deprivation among stayers, due to slight changes in neighborhoods over time, was measured. The change in deprivation among movers was then categorized into quintiles with the bottom two quintiles representing those who experienced the most decrease in deprivation and some decrease in deprivation, termed high upward mobility and mid upward mobility, respectively. The top two quintiles represented those experiencing the most increase in deprivation and some increase in deprivation, termed high downward

mobility and mid downward mobility, respectively. The middle quintile (Q3) represents those with relatively no change in deprivation but with residential mobility. This creates five deprivation mobility trajectories that are exclusive to movers. The sixth trajectory, treated as the unexposed, is that of the non-movers. The distribution of deprivation change within the non-movers relative to the movers is described in detail later to evaluate the interpretational assumption that non-movers were relatively unexposed to any change in deprivation exposure.

*Covariates*

Covariates considered as potential confounders or effect modifiers were selected based on the causal diagram and consideration of the changing impact of neighborhood deprivation throughout the life-course. These were factors that predicted both exposure to a non-stationary residential mobility trajectory and preterm birth at the second record. Confounding would be adequately controlled for if all predictors of trajectory that were also individual risk factors or predictors of individual risk factors for preterm birth at follow-up, in addition to neighborhood at baseline, were controlled for. If neighborhood at baseline were not controlled for, controlling for preterm birth at baseline in addition to the predictors of trajectory would be sufficient. Controlling for both baseline preterm birth and neighborhood allows for some control of unmeasured confounding due to incomplete control of the predictors of trajectory, such as individual SES. When the variables measured are fit into this framework, the set of covariates to be considered includes the baseline measures of maternal education, race, age, age-squared, Medicaid

payment, smoking or drinking alcohol during pregnancy, parity, adequacy of prenatal care received, marital status, preterm birth, neighborhood, and neighborhood deprivation quintile. In addition, the number of years between baseline and follow-up was measured as a rough measure of the inter-birth interval, although this has some potential of being influenced by the exposure. The measurement of each of these is briefly reviewed in the following paragraphs.

Maternal education was measured as self-reported highest grade completed on the 1st record, categorized as <9th grade, 9th-11th grade, High School diploma/GED, or at least some college. This variable was very complete, with only 4,020 (2.4%) records not reporting the measurement. Paternal education, on the other hand, was missing on 30,593 (17.9%) of records and was thus not considered a viable covariate.

Maternal race was measured on the first record as one of six categories: White, Black or African American, Asian, American Indian/Alaska Native, Native Hawaiian/Pacific Islander, and Multiracial. White and Black accounted for 95.2% of women. Based on this, the other categories were collapsed to an 'Other' race category. Whether this was self-reported race or the race as perceived by whoever filled out the birth record is unknown and likely varies. This variable was also complete, missing on no records. A comparison of race at 1st and 2nd records showed rare discrepancies between the two, but in order to treat race as time invariant, only race at 1st record was considered.

Maternal age and age-squared were measured as age at last birthday. Age-squared was included in analysis due to the previously discussed U-shaped curve of preterm birth risk with age,[34] indicating the assessment of and control for a quadratic rather than linear association may be more accurate.

Medicaid payment was measured as a rough marker of individual socio-economic status. The variable corresponds to the entity responsible for payment for hospital services at the first birth. The 18 possible payers were collapsed to Medicaid, if the payer was Medicaid Managed Care or Medicaid, or if the woman was a Medicaid Applicant, and Non-Medicaid, including all other payers. This variable was complete for the full cohort.

Alcohol and tobacco use during pregnancy were self-reported as either yes or no for each. Alcohol was missing for 787 (0.5%) while tobacco was missing for 771 (0.5%). The positive predictive value of these measurements is likely high since a false positive seems somewhat unlikely. However, the negative predictive value is likely quite low and it is possible that no use was recorded when the question was not asked.

Parity, or number of births prior to the first recorded birth, was measured as a count of the number of live births a woman had throughout her life. While the value recorded on the birth record includes the birth represented by that record, this birth was subtracted for ease of interpretation. Only 53 (0.0%) of records were missing this measurement.

Similarly, the number of unrecorded births between birth records was estimated by subtracting the parity at the first record from the parity at the second. The majority of women (89.4%) had no unrecorded births. Of the remainder, 7,867 (4.6%) had one unrecorded birth and 1,461 (0.9%) had two or more. 8,768 (5.1%) had implausible or values, such as when parity at follow-up was recorded as less than parity at baseline. These were set to missing.

The adequacy of prenatal care was measured by the Kotelchuck index which is defined by the month of entry and the number of prenatal visits (relative to the gestational age of the infant at birth). The index categorizes adequacy as inadequate, intermediate, adequate, or adequate plus. This measure was missing for 11,699 women (6.8%).

Marital status was defined as the legally recognized marital status at delivery as self-reported. Categories such as widowed and divorced were collapsed to unmarried, creating a dichotomous variable that was missing for only three women (0.0%).

Preterm birth at the baseline was measured based on the reported weeks of gestation, with preterm defined as less than 37 completed weeks. This variable was not missing for any women.

No neighborhood-level confounders aside from baseline deprivation were considered. The comparison of fixed effects and random effects models in the analysis can evaluate the plausibility of this assumption. Potential confounders that were not addressed are trajectory types related to neighborhood deprivation trajectory. For example, if the trajectory of neighborhood violent crime exposure is associated with the neighborhood deprivation mobility trajectory, the violent crime trajectory may confound the association between the mobility trajectory and the outcome.

### *Hypothesized Interactions*

On the basis of the literature reviewed and the conceptual model, five main interactions with deprivation trajectory are considered. These are race, baseline deprivation, prior preterm birth, maternal age, and inter-birth interval. The majority of

studies reviewed reported race specific estimates of the association between neighborhood deprivation and preterm birth, generally reporting stronger associations among black women compared to white. The relation between race and upward or downward trajectory association with preterm birth is relatively unknown since adult deprivation trajectories have not been previously studied. For consistency with the literature, race stratified effect estimates are analyzed and reported where significant, substantial differences were found. Baseline preterm birth is included based on the significance of the interaction between prior preterm birth and cumulative deprivation exposure in a previous study based on the same dataset as this study.[51]

The other three interactions are motivated more by the particular research question of this study and the conceptual considerations leading to our hypothesis. The baseline deprivation interaction with upward or downward mobility is important to assess as it seems likely that the effect of a decrease in deprivation by a given amount would depend on the starting level of deprivation. The interaction would not be expected if deprivation is actually a continuous variable and the association between deprivation and preterm birth is linear. However, a non-linear association such as a sigmoidal or threshold function may be more likely. Moving to worse deprivation may have a smaller relative impact on preterm birth risk among those with high baseline deprivation than among those with mid baseline deprivation. Similarly, moving to less deprivation may have a smaller impact among those with already low baseline deprivation than among those with mid or high baseline deprivation.

The assessments of interactions with age and inter-birth interval are motivated by the life-course considerations discussed in the literature review. It is hypothesized that

risk of preterm birth increases with increasing duration of exposure to neighborhood deprivation. Age at baseline is conceptualized as a marker of prior exposure duration. The effect of moving to lower or higher deprivation could depend on the amount of accumulated exposure prior to the move. Another perspective is that the risk accumulated with age could become harder to erase, such as by a move to a lower deprivation area, as age increases. While this study cannot offer much in terms of specifying the underlying risk accumulating mechanism, an interaction with age would provide evidence for further study. Similarly, the association between deprivation trajectory and preterm birth could depend on the amount of time lived in the increased or decreased deprivation neighborhood. The effect of a change in deprivation is not likely to be immediate and is expected to take several years to embody itself in preterm birth risk. For this reason, the effect of an increase or decrease in deprivation is expected to be greater for women with greater time between births, under the assumption that these women have lived in the new neighborhood for longer periods of time than women with shorter inter-birth intervals. This assumption is not testable given the data, but again, the identification of an interaction would provide evidence for further study.

*Analytic Methods*

The analytic strategy used was to consider the women as clustered in baseline neighborhoods and estimate the associations between mobility trajectories and risk of preterm birth, drawing comparisons between women in the same baseline neighborhood with women who did not move neighborhoods between births as approximating the

counterfactual. That is, it is assumed that, all else being equal, the outcome experienced by the non-movers was that which would have been experienced by the movers, regardless of particular trajectory, had they not moved. Mobility trajectories were considered as individual characteristics. The neighborhood clustering and between-neighborhood variability is primarily considered a nuisance rather than an aspect to be estimated and explained. However, since it was hypothesized that the effect of deprivation trajectory may depend on the baseline neighborhood deprivation level, the neighborhood-level variation in the outcome is modeled to test this cross-level interaction.

*Cohort Definition and Descriptive Statistics*

The target population was all women having two or more births while residing in the 10-county Atlanta Metropolitan area during the years 1994 through 2007. This was sampled from a population based sampling frame that included all birth records in the state of Georgia during the time period that could be linked maternally so that sibling pairs were linked when multiple births to the same woman were present. These were then geocoded based on the residential address listed on the birth record. This excluded women with addresses that could not be geocoded at the street-level. This included 1,815,944 birth records linked to 1,261,039 mothers. This set was restricted to mothers with at least two births with the second birth being singleton. It was further limited to the first two consecutive births for each mother, as measured by the recorded year on each record, resulting in 782,678 births linked to 391,339 women. Temporal ordering of birth

records was necessary for proper trajectory measurement. This ordering was done by birth year when birth years differed between sibling pairs. For siblings born in the same year (n=1,796 births), the parity at each birth was used to assign temporal order. If the parity did not show a clear order, such as when the parity at each birth was identical or consecutive, the temporal order could not be assigned and these women were excluded (n=1,572 births). The total set of birth pairs included 781,106 births to 390,553 women. The geocoded birth pairs were then restricted to those in the Atlanta Metropolitan Area as defined by the ten county region including Cherokee, Clayton, Cobb, DeKalb, Douglas, Fayette, Fulton, Gwinnett, Henry and Rockdale counties and as measured by the residential county code on the birth record. This resulted in a final cohort of 170,865 women with 2 births each.

Descriptive statistics were calculated for each mobility trajectory, each covariate, and the preterm birth outcome. In addition, the number of observations, exposures, and outcomes for each neighborhood was calculated and summarized to ensure adequate within-neighborhood sample size and an adequate number of neighborhoods for the planned regression strategies.

*Regression Model Structures*

Primary analyses were conducted using fixed effects and random effects conditional logistic regression models and marginal generalized estimating equations models. Each of these provides estimates with slightly different interpretations and

underlying assumptions.[57-59] The results from these three methods were compared to gauge consistency of estimates across model structures.

The fixed effects conditional model is intuitively closest to the desired strategy of comparing women with mobile and non-mobile trajectories who shared a neighborhood at baseline. It is similar in structure to the analysis used for matched analyses, except only baseline neighborhood is matched on. This model estimates and conditions on a parameter for each neighborhood, leading to less statistical efficiency than the random effects model which treats these parameters as a random variable. The model structure, without specific covariates, is shown in equation 1. Fixed effects models are fit through SAS's PROC SURVEYLOGISTIC with the neighborhoods used to define clusters and entered as dummy variables into the models.

$$Y_{ij} = \beta_0 + \boldsymbol{\beta}(MT)_{ij} + \boldsymbol{\gamma}(V)_{ij} + \boldsymbol{\delta}(W)_{ij} + \sum \gamma_j Tract_j + \varepsilon_{ij}$$

Equation 1. Fixed Effects Model Structure. $Y_{ij}$ is the log(odds) of preterm birth for women 'i' living in baseline neighborhood 'j'. MT is the set of mobility trajectories. V is the set of individual confounding variables. W is the set of interactions. Each neighborhood, or tract, is entered into the model as a dummy variable such that estimates of odds are conditional on the specific baseline neighborhood of residence, ensuring that comparisons are between women sharing a baseline neighborhood.

The random effects model is a conditional model, similar to the fixed effects model. However, it does not estimate a parameter specific to each neighborhood and is therefore more efficient than the fixed effects model. To avoid this estimation, the neighborhood indicator variable is considered to be random rather than fixed. Assumptions are then made about the mean and variance of this random 'intercept.' While this leads to increased efficiency when the assumptions hold, it leads to

inconsistent estimation of main effects when the assumptions are violated. The strength of the assumptions can be tested using the Hausman test, which compares the consistency of the random effects model estimates to the fixed effects model.[59] Beyond efficiency, the random effect model allows for inclusion of neighborhood-level independent variables while the fixed effects model does not. For this study, the baseline neighborhood deprivation is the only relevant and measured neighborhood level variable. The degree to which the baseline deprivation explains variation in the effect of deprivation trajectory between neighborhoods can be estimated by the random effects model through the assessment of the cross-level interaction between baseline deprivation and mobility trajectories. These models are fit using SAS's PROC GLIMMIX with a random intercept for each neighborhood. The form of the model is presented in equation 2.

$$Y_{ij} = [\boldsymbol{\beta}(MT)_{ij} + \boldsymbol{\gamma}(V)_{ij} + \boldsymbol{\delta}(W)_{ij} + \varepsilon_{ij}] + [\gamma_{00} + \boldsymbol{\gamma}_{0i}(DQ)_{0j} + \mu_{0j}]$$

$$\mu_{0j} \sim N(0, \tau_0)$$

Equation 2. Random Effects Model Structure. $Y_{ij}$ is the log(odds) of preterm birth for women 'i' living in baseline neighborhood 'j'. MT is the set of mobility trajectories. V is the set of individual confounding variables. W is the set of interactions. The neighborhood-level component is estimated by the second component where DQ is the baseline deprivation quintiles. There is both a neighborhood specific, individual level error term ($\varepsilon_{ij}$) and a neighborhood-level error term ($\mu_{0j}$). It is assumed that this later error term is distributed normally with mean zero and variance $\tau_0$. The covariance structure was assumed to be compound symmetric since the correlation between individuals within neighborhoods was assumed to be equal across all individuals in that neighborhood.

The marginal model utilizes generalized estimating equations rather than maximum likelihood estimation. There has been considerable debate in recent years over the relative merits of marginal models and random effects models.[57, 58] The core

interpretational difference for individual-level associations seems to be that between estimating the average within-neighborhood individual-level odds ratio and estimating the average of the neighborhood-level odds ratio, which are the average of individual odds ratios specific to each neighborhood. This is the difference between averaging estimates across the population of neighborhoods and averaging estimates across the population of individuals. Both seem to be relevant public health inferences depending on the type of intervention considered and level of inference desired: an individual-level inference connected with an individual-level intervention such as assigning mobility trajectories to individuals would be better made through a marginal model; a neighborhood-level inference connected with a neighborhood-level intervention such as assigning mobility trajectories to entire neighborhoods (such as through neighborhood redevelopment projects would be better made through a neighborhood specific random or fixed effects model. Since both of these estimates can be made given the data in this study, both models are fit and reported. The marginal models were fit with SAS's PROC GENMOD with the neighborhood as the subject in the REPEATED statement.

$$E_j(Y_{ij}|\ Tract_j) = \beta_0 + \boldsymbol{\beta}(MT)_{ij} + \boldsymbol{\gamma}(V)_{ij} + \boldsymbol{\delta}(W)_{ij} + \boldsymbol{\gamma}_j Tract_j + \varepsilon_{ij}$$

$$\gamma_j \sim N(0, \sigma)$$

Equation 3. Population Average Model (Marginal Model) Structure. $Y_{ij}$ is the log(odds) of preterm birth for women 'i' living in baseline neighborhood 'j'. MT is the set of exposure trajectories. V is the set of individual confounding variables. W is the set of interactions. An intercept, $\gamma_j$ is estimated for each neighborhood and the set of neighborhood intercepts is assumed to be normally distributed with mean zero and variance $\sigma$. The tract specific odds are averaged across the population of neighborhoods for the final estimates, thus the estimate is the population average log(odds) rather than individual log(odds).

*Modeling Strategy*

To find the best fitting model, a modeling process starting with collinearity assessment and moving to interaction then confounding and finally precision assessments was followed. The initial independent variables entered into the models are those identified through the literature review and study design. These are the six categories of mobility trajectory (high upward, mid upward, no change but mobile, mid downward, high downward, and non-mobile), baseline neighborhood deprivation quintile, inter-birth interval, and the set of individual-level predictors of exposure measured at baseline (maternal age, age-squared, marital status, alcohol use during pregnancy, tobacco use during pregnancy, education, prenatal care adequacy, preterm birth, Medicaid payment, parity, and race). The modeling strategy was applied separately for the marginal and conditional models.

Collinearity, which is a problem that arises when independent variables in a regression model are highly correlation with one another, was assessed in a model fit with all covariates as well as the interactions between each exposure and covariate. The condition indices (CIs) and variance decomposition proportions (VDPs) was calculated to identify collinearity problems. Cut points for collinearity problems are CIs greater than 20. Variables involved in the problem are those with VDPs greater than 0.5. Interaction terms involved in collinearity problems were dropped from the model prior to confounders. Socio-demographic confounders were given preference over other individual-level covariates because these are likely most strongly associated with mobility trajectories.

The remaining variables not involved in collinearity problems were then assessed for interaction. This was primarily done through the fixed effects model since this model uses maximum likelihood estimation, allowing quantitative comparisons of model fit through likelihood ratio tests of nested models, which cannot be calculated with the GEE based marginal model, and makes fewer assumptions about the covariance structure than the random effects model. A likelihood ratio test of each individual interaction was used to identify possibly significant interaction terms. After dropping interactions that are not individually significant relative to the full model, all possible subsets of significant interactions were tested relative to the full model. The smallest subset that provides the equivalent fit of the full model was considered as containing only significant interactions, provided they were also significant based on the Wald Chi-square statistic.

Covariates that do not interact with the exposures were then assessed following a backwards elimination strategy. Those that can be removed with a less than 10% change in mobility trajectory associations with preterm birth were removed unless the precisions of these estimates are significantly changed. Removing these unnecessary covariates increases model parsimony.

The final model identified through this strategy was then fit in both the conditional and marginal models and reported in comparison to the crude model containing only exposure and baseline deprivation, aside from the fixed effects model which precludes conditioning on neighborhood baseline deprivation by conditioning on neighborhood. The fixed effects and random effects models were then compared using the Hausman test, which tests the consistency of the random effects model relative to the fixed effects model.

*Model Fit and Validity Assessment*

The diagnostics of the final model were assessed using residual analysis to assess the model specific assumptions, receiver operating characteristic curves to assess model discrimination, and an analysis of the separation of the data points. The impact of any separation of data points was assessed through comparisons of the final models to models fit using propensity score techniques.

The validity of the final model was assessed through comparisons of the final model estimates to estimates calculated through inverse propensity weighting. The issue addressed by propensity score methods is that not all individuals have non-zero probability of each mobility trajectory, much less equal probability, as would be the case in a randomized trial. It is the assumption of any effect estimate that all individuals have a non-zero probability. Propensity scores are the estimated probability of specific mobility trajectories based on the non-exposure covariates. This may be different from the actual propensity due to unmeasured confounding variables. However, if an estimated propensity score is zero or one, then the covariate pattern that produced that propensity score violates the condition that all individuals have a non-zero probability of each exposure type. By weighting the regression model by a weights based on the propensity scores the model can be specified such that individuals with zero probability of being exposed to a trajectory other than the one which they were actually exposed to receive no weight in the regression, effectively excluding them from the analysis and avoiding the non-zero probability of exposure problem. However, this method is not perfect as the set

of individuals producing effect estimates excludes some covariate patterns that were of interest and the new set may be more difficult to define than the full set, making extrapolation to the target population difficult. These propensity score methods were applied separately for each mobility trajectory, comparing those with that trajectory to the non-mobile trajectory and defining propensity scores only in the cohort that experienced either of these two trajectories.

## Results

*Descriptive Statistics*

The follow-up preterm birth prevalence in the full cohort was 10.14%. This varied significantly by deprivation mobility trajectory. Among those who experienced high upward mobility the preterm birth prevalence was 11.65%. Among those with an intermediate level of upward mobility the preterm birth prevalence was 10.37%. Among those who moved but did not undergo a change in deprivation exposure the preterm birth prevalence was 9.50%. The prevalence among those with an intermediate level of downward mobility was 10.32%. For women undergoing high downward mobility the preterm birth prevalence was 12.31%. Those who stayed in the same tract had a prevalence of 9.36%. (Table 1)

These measures are not entirely meaningful without taking into account the baseline tract, from which the deprivation trajectories were measured. This was done through measuring the above prevalences within each tract and then averaging these across all 564 tracts. Overall, the preterm birth prevalence varied strongly between tracts. The mean prevalence was 10.6% (Standard Deviation, SD, 3.9%) and ranged from 1.4% to 30.9%. Within tracts, the prevalence differed by deprivation mobility trajectory. Averaged across all tracts, the preterm birth prevalence was 11.86% (SD 6.42%) among those who did not move between births. The average within-tract prevalence among those with high upward mobility was 12.74% (SD 11.80%). Those with intermediate upward mobility had an average prevalence of 13.63% (SD 19.82%). Those who moved but did not change deprivation had an average prevalence of 14.24% (SD 19.90%). Those with

the intermediate level of downward mobility had an average prevalence of 13.76% (SD 14.50%). The groups undergoing high downward mobility had an average prevalence of 16.27% (SD 17.07%). A rough trend of increasing average prevalence from the high upward to the high downward mobility groups can be seen here. (Tables 2A,B)

The within-tract preterm birth prevalences by exposure categories were used to calculate rough within-tract risk differences and risk ratios that were then averaged across tracts. While these provide evidence in support of the regression based conclusions, they are flawed in that they do not take the differing sizes of tracts (Mean 304 (SD 193), Min 20, Max 1534, N 564) into account and do not allow the precision of the average estimates to be assessed. Rather, they provide distributions of risk differences and risk ratios that can be simply summarized by a mean and standard deviation. The referent group for each within-tract risk difference or risk ratio is that tracts women who did not move between births, who did not substantially change deprivation exposures. The average risk among those with high upward mobility was decreased by 1.77% compared to stayers (SD 11.26%) (average RR 0.98 (SD 1.07)). The average risk among those with intermediate upward mobility was increased by 0.89% (SD 18.92%) (average RR 1.20 (SD 2.19)). Among those who moved with no change in deprivation, the average risk was increased by 2.53% (SD 18.86%) (average RR 1.35 (SD 1.67)). The average risk among those with intermediate downward mobility was 2.18% (SD 13.69%) (average RR 1.30 (SD 1.34)). Those with the greatest downward mobility had the greatest average increase in risk at 4.30% (SD 16.31%) (average RR 1.59 (SD 1.82)). On average, the preterm birth risk was lower for those moving to a much less deprived tract relative to those who did not move for women who shared a tract at baseline; while the risk was higher for those

moving to a more deprived tract relative to the same stayer groups. These results are preliminary at this point, but provide simple stratification based evidence in support of the regression based estimates to follow. (Table 2B)

Before moving into regression modeling, the mobility trajectory and covariate distribution in the cohort are reviewed here. The cohort was divided into six possible deprivation mobility trajectories: Stayers, High Downward, Intermediate Downward, No Change, Intermediate Upward, and High Upward. All but the stayers were categorized based on the distribution of change in deprivation among movers through dividing this distribution into quintiles. Overall, 53.0% of the cohort moved census tracts between births. This proportion varied by baseline tract. The average proportion moving per tract was 53.4% (SD 14.8%) and ranged from 16.5% to 90.7%. Importantly, all tracts had at least some stayers, allowing a referent group to be defined within each tract. The global prevalence of the mobile exposure trajectories was equal, at 10.60%, since these were defined based on quintiles of the distribution of change in deprivation among movers. However, the prevalence differed between tracts and some tracts did not have individuals with all mobility trajectories. These distributions of prevalences are summarized by their mean, standard deviation, minimum, and maximum in table 3.

The deprivation mobility trajectories came from the distribution of continuously measured change in deprivation among movers. These trajectories are then compared to stayers, who did not substantially change deprivation exposure relative to movers. However, there was some change in deprivation among stayers since tracts are not static and deprivation levels changed through time. This change was captured through the linear interpolation of deprivation measures at three different years. The distributions of

change in deprivation among movers and among stayers in the cohort provide support for the interpretation of stayers as not substantially changing deprivation relative to movers. Among movers, the mean change in deprivation was 0.14 (SD 0.90) and the inter-quartile range was from -0.32 to 0.59. Among stayers, the mean change in deprivation was 0.03 (SD 0.15) and the inter-quartile range was from -0.03 to 0.06. While the means of the two distributions are relatively similar, given the range of deprivation change is from -5.58 to 5.39, there was much more variation among movers than stayers as indicated by the 6 fold increase in standard deviation and much wider inter-quartile range. The range of change in deprivation values within each mobility trajectory were as follows: High upward mobility ranged from 5.39 to 0.74. Intermediate upward mobility ranged from 0.73 to 0.29. No-change ranged from 0.28 to -0.03. Intermediate downward mobility ranged from -0.04 to -0.45. High downward mobility ranged from -0.46 to -5.58.

While the change in deprivation, as measured by the Neighborhood Deprivation Index, was used to define mobility trajectories, the change in poverty rate of the tract that accompanies a change in deprivation may be more interpretable. Those with high upward mobility experienced an average decrease in tract poverty rate of 14% (SD 13%). Among the intermediate upwardly mobile, the tract poverty rate decreased by 4% on average (SD 5%). Those with no change in deprivation experienced a 1% or less change in poverty rate, on average. Those with intermediate downward mobility experienced an increase in poverty rate of 2% on average (SD 4%). Those with high downward mobility experienced an average increase in poverty rate of 10% (SD 10%). The non-mobile did not experience any significant change in poverty rate.

Baseline deprivation differed greatly between mobility trajectory groups. Part of this was due to the nature of the exposure: the number of potential tracts a person can move to in order to have a specific mobility trajectory varies as a function of the baseline deprivation. For example, those with the least deprived baseline deprivation have very few, if any, potential tracts to move into where they could experience the high upward mobility trajectory, resulting in low proportions of individuals with upward mobility trajectories in the low deprivation tracts. Likewise, those with the most deprived baseline deprivation have few options for worse tracts to move into and therefore very low probability of experiencing the high downward mobility trajectory, with only 14.7% of those experiencing high downward mobility living in a high deprivation baseline neighborhood while 66.2% of the highly upwardly mobile lived in a high deprivation baseline neighborhood. (Table 1)

Baseline deprivation was also strongly associated with the preterm birth outcome. This was expected as it is approximately the crude statistic calculated by cross-sectional studies of tract deprivation and preterm birth. The least deprived quintile had an average preterm birth prevalence of 7.3% (95% Confidence Interval 6.73%, 7.85%). The most deprived had an average prevalence of 13.91% (95%CI 12.8%, 15.1%). The odds ratio comparing the low deprivation quintile to the high deprivation was 0.49 (95%CI 0.47, 0.52). The quintiles between these extremes had intermediate average prevalences: 8.41% in mid-low deprivation, 9.80% in mid, and 11.29% in mid-high deprivation. (Table 2A)

Other covariates were all significantly individually associated with preterm birth, but were not as strongly associated with the mobility trajectories as baseline deprivation. The statistical significance is likely a product of the large sample size in many cases, so

the strength of the association should be taken into account for each of the covariates. The covariates individual-level covariates considered were the inter-birth interval length and the following all measured at the first birth: maternal age, age-squared, education, race, Medicaid payment for first birth, marital status, parity, alcohol use during pregnancy, tobacco use during pregnancy, adequacy of prenatal care, and preterm birth. (Table 1)

Maternal age differed somewhat between mobility trajectories. Stayers tended to be slightly older than those in any of the mobile exposure trajectories. Those with upward trajectories tended to be somewhat older than those with downward trajectories. Age was associated with preterm birth through the familiar U-shaped curve, best modeled by a quadratic function of age. The greatest preterm birth risk was in the lowest age group (<15 years), which had a 16.5% prevalence. The lowest was in the 30-34 year category at 8.7%, with a slight rise in risk in older women: 10.2% for those aged 35-39 years.

The inter-birth interval also showed a U-shaped association with preterm birth. Women with a very short (<1 year) inter-birth interval had a very high prevalence of preterm birth (37.4%). This prevalence dropped as the inter-birth length increased to a low of 8.9% among those with three or four years between births. After this the prevalence increased again to 10.7% at five or six years and 12.8% at seven or more years. It was expected that increased time between births would be associated with increased mobility, following an accumulation of mobility opportunities with time. This was confirmed as stayers tended to have shorter inter-birth intervals than those with mobile trajectories. 58% of stayers had less than three years between births while 41% of movers had less than three years. Among mobile trajectories, the distribution of inter-

birth intervals was relatively homogenous, with a slight tendency towards longer intervals among the decreasing deprivation trajectories relative to the increasing deprivation trajectories.

In comparison to the full cohort racial composition, white women were more likely to experience the non-mobile, no change, or intermediate downward trajectories than the upward trajectories or the high downward trajectory. Black women were more likely to experience the high upward, intermediate upward, or high downward trajectories than the non-mobile, no change, or intermediate downward trajectories. Race was significantly associated with preterm birth, with black women having a prevalence of 14.2% while white women had a prevalence of 7.9% (OR 1.63 (95%CI 1.55, 1.72)).

The educational composition of each mobility trajectory also differed. Those with less than a high school education tended to be in either the high upward or high downward trajectories in comparison to the other trajectories. Those with only a high school education or GED were more likely to be in the high upward or high downward trajectories, but the differences in percentages within each trajectory were not widely different (range 20% in stayers to 31% in most increased). Those with some college education were more likely to be in the non-mobile or no change trajectories and most unlikely to be in the high upward or high downward trajectories. The preterm birth prevalence was greatest among those with a $9^{th}$-$11^{th}$ grade education, at 13.6%, and least among those with some college (8.3%). The odds ratio comparing the $9^{th}$-$11^{th}$ grade group to the some college group was 1.38 (95%CI 1.31, 1.45).

Women who used Medicaid to pay for their 1st record births were most likely to experience the high downward mobility trajectory (56% compared to 35% of the full

cohort) or the high upward mobility trajectory (53% compared to 35% of the full cohort). Medicaid users were least likely to be in the non-mobile trajectory (24% compared to 35%). The preterm birth prevalence was greater among Medicaid users (12.6%) compared to 8.8% among those with other payers (OR 1.21 (95%CI 1.16, 1.26)).

Parity at the first birth record did not appear to differ meaningfully between mobility trajectory groups. However, parity was associated with preterm birth, with risk increasing as parity increased. The prevalence among those whose 1st record was their first birth was 9.4% and increased to 11.1% for the 2nd birth, 12.3% for the 3rd, and 16.3% for the 4th or higher.

Women who were married at their 1st recorded birth were most likely to experience the non-mobile trajectory (79% of stayers were married compared to 69% of the full cohort). Married women were less likely to experience the high upward or high downward trajectories (51% and 47% compared to 69% in the full cohort, respectively). Married women were also significantly less likely to deliver the 2nd birth preterm. The preterm prevalence among the married was 8.3% compared to 14.2% among the unmarried (OR 0.68 (95%CI 0.65, 0.71)).

Tobacco and alcohol use during pregnancy were relatively rare in this cohort (4.5% and 0.9% respectively), which may be a product of poor measurement. Alcohol use didn't seem to substantially vary between mobility trajectories. Tobacco use was slightly more prevalent among those with downward mobility than among the upwardly mobile. The odds ratio for preterm birth by alcohol use was 1.49 (95%CI 1.28, 1.73). The odds ratio for tobacco use was 1.51 (95%CI 1.41, 1.62).

Prenatal care adequacy did not differ substantially between mobility trajectories. However, prenatal care was associated with preterm birth. Those with inadequate prenatal care had a prevalence of 13.7% compared to 8.0% among those with intermediate or adequate prenatal care (OR 1.55 (95%CI 1.43, 1.67)). Those with adequate-plus prenatal care had a higher prevalence of preterm birth as well, at 12.9% (OR 1.67 (95%CI 1.56, 1.78). This may have been a product of underlying medical risk factors.

Preterm birth at the baseline birth was not substantially associated with mobility trajectories. The prevalence among stayers was 9.3%. Among movers with no change in deprivation the prevalence was also 9.3%. Among those with high downward or high upward mobility the prevalence was 11.3% and 11.0% respectively. Prior preterm birth may be a substantial confounder although it is only mildly associated with exposure because it is strongly associated with preterm birth at the 2$^{nd}$ record. The prevalence of preterm birth at the follow-up birth among those without a preterm birth at baseline was 8.4% compared to 26.1% among those who had a preterm birth at baseline (OR 3.68 (95%CI 3.51, 3.83)). (Table 1)

Given that each of the covariates discussed above was associated with both exposure and outcome with statistical significance and all were substantially associated with follow-up preterm birth, although not necessarily with the mobility trajectories, each was considered as a potential confounder in the modeling process. Since the covariates were not evenly distributed between tracts, resulting in clustering of covariates within tracts, a modeling process was used that took this clustering into account. (Table 3)

Following the modeling strategy previously described, a final model was constructed that included the same variables for each of the model structures aside from the exclusion of baseline deprivation in the fixed effects model. A parameter was estimated for each of the five mobile exposure trajectories. Confounders adjusted for included maternal age and education as well as the lower-order terms of each of the interactions. Interactions between mobility trajectories and maternal age, inter-birth interval length, and prior preterm birth were included as well. Taking the dummy-variable coding scheme into account for categorical variables, this resulted in a model with 28 parameters, with an additional four corresponding to the baseline deprivation quintiles.

*Regression Model Results*

The fixed effects model is considered the gold standard between the three model structures as it provides estimates that can be interpreted in a way that provides a closer answer to the original research question than the marginal model does and makes fewer assumptions than the random effects model does. The marginal model provides population average estimates which may be of interest and is interpreted in comparison to the conditional model results. The random effects model has greater statistical efficiency than the fixed effects model and therefore may provide more precise answers. For these reasons, the results of all three model structures are reported.

*Crude Model Results*

Crude measures of association between each mobility trajectory and preterm birth were calculated through each of the model structures. (Table 4) Each model structure estimated crude associations roughly in line with the hypothesis. In the fixed effects regression model, the high upward mobility trajectory was associated with decreased odds of preterm birth (OR 0.84 (95%CI 0.80, 0.88)) while the high downward mobility trajectory was associated with increased odds of preterm birth (OR 1.22 (1.17, 1.27)). The trajectory with intermediate downward mobility was associated with increased odds of preterm birth, but with slightly lower magnitude (OR 1.09 (1.04, 1.15)). The trajectories with intermediate upward mobility or no change in deprivation were not significantly associated with preterm birth in the crude fixed effects analysis (ORs 0.95 and 0.98, respectively). Odds ratios from the fixed effects model represent the average within-tract associations for the specific set of tracts examined in this cohort.

In the crude, baseline deprivation adjusted random effects model, the trajectory estimates were similar to the crude fixed effects estimates, with some minor differences. The odds ratio for high downward mobility was slightly greater than the fixed effects estimate, at 1.30 (95%CI 1.24, 1.37). Likewise, the odds ratio for the intermediate downward mobility trajectory was 1.14 (95%CI 1.08, 1.20) compared to 1.09 from the fixed effects model. The odds ratios for the no-change and intermediate upward mobility trajectories were not significant (1.02 and 0.98, respectively). The odds ratio for high upward mobility was 0.90 (0.85, 0.95), slightly closer to the null than the fixed effects estimate of 0.84. Odds ratios from the random intercept model represent the average

within-tract associations assuming the tracts observed in this study were a sample from a much larger population of tracts.

Marginal model crude results, adjusted for baseline, were again very similar to the fixed and random effects estimates, with slightly greater similarity to the random effects estimates than the fixed effects estimates. The crude OR for the high upward mobility trajectory was 0.90 (95%CI 0.85, 0.95). The intermediate upward and no-change trajectories were not significantly associated with preterm birth (ORs 0.98 and 1.02, respectively). The intermediate downward trajectory was associated with 1.16 times the odds of preterm birth (95%CI 1.09, 1.22). The high downward mobility trajectory had an OR of 1.32 (95%CI 1.25, 1.39). Odds ratios from the marginal model represent the population average association of the mobility trajectories with the outcome, averaged across individuals instead of averaged across tracts, while still accounting for tract clustering.

*Final Model Results*

The final model results are reported here at the mean value of interaction terms. (Table 4) That is, the summary odds ratios for the final model are for maternal age 26 at baseline, three year inter-birth interval, and no preterm birth at baseline. The final fixed effects model estimates were generally shifted slightly towards the null compared to the crude estimates and did not remain significant for some mobility trajectories. The odds ratios (95%CIs) comparing each of the trajectories to women in the same tract who stayed were as follows: high upward 0.93 (0.88, 0.98), intermediate upward 0.98 (0.93,

1.04), no change 1.00 (0.94, 1.06), intermediate downward 1.04 (0.98, 1.09), and high downward 1.15 (1.09, 1.21). The high upward and downward trajectories are still significantly associated with preterm birth (high upward only slightly), but other trajectories are no longer significant.

The random effects and marginal models produced similar final model estimates, shifted towards the null from their respective crude associations. In comparison to the fixed effects estimates, the random effects and marginal estimates were shifted towards the null for the upwardly mobile and away from the null for the downwardly mobile. The random effects final model estimates were as follows: high upward OR 1.01 (95%CI 0.94, 1.08), intermediate upward OR 1.04 (95%CI 0.97, 1.11), no change OR 1.06 (95%CI 0.99, 1.13), intermediate downward OR 1.10 (95%CI 1.03, 1.18), and high downward OR 1.21 (95%CI 1.13, 1.30). The final marginal model ORs (95%CIs) were: high upward 1.01 (0.94, 1.08), intermediate upward 1.04 (0.97, 1.11), no change 1.06 (0.99, 1.13), intermediate downward 1.10 (1.03, 1.18), and high downward 1.21 (1.14, 1.30). The estimates of the random effects and marginal models are nearly identical.

*Interactions*

Statistical interactions were first identified through regression modeling based methods. These included interactions between deprivation trajectories and maternal age at baseline, inter-birth interval length, and prior preterm birth. The interactions were not uniform in strength or direction for each mobility trajectory. They are reported here based on the final fixed effects conditional model results. (Figures 4, 5, and 6, Table 5)

Maternal age was included in the models as quadratic, with an age and age-squared term. The interaction between age-squared and mobility trajectories was not significant after the inclusion of the linear age and mobility trajectory interaction. Thus, while the risk of preterm birth associated with age is best modeled by a quadratic function, with highest risk among younger and older women, the interaction between mobility trajectories and age is roughly linear, implying a constant rate of change of the risk associated with each mobility trajectory with increasing age. The change in age-specific exposure odds ratios when the quadratic interaction was kept in the model was assessed and found to not change the estimates far from linearity. Given the non-significance of the quadratic interaction and the strong significance of the linear interaction, no further forms of the interaction between age and exposures were assessed.

Based on the fixed effects final model, the association between the high upward mobility trajectory and preterm birth was strongest at the youngest maternal age and decreased in magnitude towards the null as age increased, becoming non-significant around age 35. The intermediate upward mobility trajectory was also strongest at younger ages and decreased towards the null, but was not significant at any age. The no change trajectory was non-significant at younger ages, but dropped to an odds ratio significantly below one between ages 30 and 35. The intermediate downward and high downward mobility trajectories interacted with age in opposite directions. While the intermediate downward trajectory was most strongly associated with increased preterm birth risk at younger ages and decreased towards the null as age increased, the high downward mobility trajectory had no association with preterm birth at the youngest ages and increased in magnitude as age increased. The strongest interaction, judged by the rate of

change of the trajectory odds ratio with increasing age, was between the high downward mobility trajectory and age, which was null at ages 15 and 20, but increased to a magnitude around 1.25 at the oldest maternal ages, between 35 and 40. The other trajectories odds ratios seemed to show a trend of stronger associations at younger ages and movement towards null associations as age increased.

The age and exposure interactions can be summarized quantitatively as follows. For a five year increase in age, the odds ratio for the high upward mobility trajectory is increased by 0.035. The odds ratio for intermediate upward mobility is increased by 0.018. The odds ratio for no-change is decreased by 0.0322. The odds ratio for intermediate downward mobility is decreased by 0.020. The odds ratio for high downward mobility is increased by 0.047. That is, for upward mobility trajectories, the odds ratio is less than null and increased towards the null as age increases. For downward mobility trajectories the conclusions differ. The intermediate downward mobility trajectory starts above the null and decreases towards the null as age increases. The high downward mobility trajectory starts above the null and increases further from the null as age increases.

The interaction between inter-birth interval length and mobility trajectory was less clearly linear based on comparisons of the linear estimates and the categorical estimates. However, the variation from linearity did not suggest any other trend, so the linear model, while a perhaps excessive simplification, provides the most interpretable results. The interaction between length of interval and mobility trajectory was strongest for those with high upward mobility, intermediate upward mobility, and high downward mobility trajectories and relatively non-substantial with the intermediate downward and no-change

trajectories. The upward mobility trajectories were most strongly associated with decreased odds of preterm birth at shorter inter-birth intervals, with the high upward mobility trajectory association becoming null after about a five year interval. The high downward mobility trajectory was most strongly associated with increased preterm birth odds at shorter inter-birth intervals and decreased towards the null with increasing time between births, becoming null after about five years. Quantitatively, this is an increase in the odds ratio of the high upward mobility trajectory with exposure by 0.028 for a one year increase in inter-birth interval. The odds ratio for intermediate upward mobility was increased by 0.022 for a one year increase in inter-birth interval. The odds ratio for no-change was decreased by 0.017. The odds ratio for intermediate downward mobility was increased by 0.004 and the odds ratio for high downward mobility was decreased by 0.021. This shows a rough trend of increasing odds ratios, towards the null, with increasing inter-birth interval length, for the upwardly mobile and decreasing odds ratios, also towards the null, for the downwardly mobile.

When examining the association between trajectory and preterm birth at different stratum of inter-birth intervals, rather than modeling the interaction as continuous, the conclusions were similar, although less clear. The high upward mobility trajectory did not become null until between seven and eight years inter-birth interval. The high downward mobility trajectory did not have a significant association at very short inter-birth intervals (<1 year), but subsequently had its strongest associations at 1-2 years and 3-4 years, becoming null again at 5-6 years, but rising again after six years to levels similar to the 1-2 year and 3-4 year levels.

The interaction between the mobility trajectories and prior preterm birth is the clearest since prior preterm birth is a binary variable allowing easy stratification. When the baseline birth was preterm, the odds ratio for the association between the mobility trajectory and the follow-up birth being preterm were generally increased in magnitude, away from the null, compared to when the baseline birth was not preterm. For the high upward mobility trajectory, with a preterm birth at baseline, the OR is 0.85 (95%CI 0.78, 0.94). Without a preterm birth at baseline this OR is 0.93 (95%CI 0.88, 0.98). The odds ratio does not change substantially by baseline preterm birth for the intermediate upward mobility trajectory. The no-change trajectory has an OR of 0.94 when the baseline birth was preterm, compared to 1.00 when not preterm, although neither of these is significant. For intermediate downward mobility, the OR increases from 1.04 (95%CI 0.98, 1.09) without a baseline preterm birth to 1.15 (95%CI 1.04, 1.27) when the baseline birth was preterm. The high downward mobility trajectory has associations that change in the opposite direction: without a baseline preterm birth the OR is 1.15 (95%CI 1.09, 1.21) and with a baseline preterm birth the OR is 1.09 (0.98, 1.18). While these estimates are from the fixed effects model, the random effects and marginal models produced very similar estimates. The marginal model was set to estimate risk differences instead of odds ratios through the link function. This allowed assessment of interaction for preterm birth on the additive scale. The interaction remained significant and, when the baseline birth was preterm, the risk differences were: high upward -1.09% (95%CI -3.26%, 1.88%), intermediate upward -0.13% (-2.53%, 2.28%), no-change -2.17% (-4.58%, 0.23%), intermediate downward 1.87% (-0.43%, 4.18%), and high downward 1.88% (-0.38%, 4.14%). In comparison, when the baseline birth was not preterm, the risk differences

were: high upward -0.43% (-1.01%, 0.15%), intermediate upward 0.03% (-0.47%, 0.53%), no-change 0.30% (-0.18%, 0.77%), intermediate downward 0.64% (0.16%, 1.11%), and high downward 1.30% (0.73%, 1.88%). Interestingly, only the downward mobility trajectories when the baseline birth was not preterm remain significant in the marginal model estimating risk differences. None of the associations were significant when the baseline birth was preterm.

*Model Fit and Discrimination*

Before interpreting any of these results further, the fit of each model is addressed and compared between model types. The model goodness-of-fit and discrimination was assessed primarily for the fixed effect model and assumed to be somewhat similar for the marginal and random effects model when aspects of fit could not be calculated for these models.

The fit of the fixed effects model was assessed through the Hosmer-Lemeshow test which summarizes the closeness of each predicted probability to the observed probability in the fully parameterized model. The null hypothesis for the test is that there is no evidence of lack of fit in the model. The alternative is that there is evidence of lack of fit. The p-value for the Hosmer-Lemeshow test of the final fixed effects model was 0.032, indicating that the null hypothesis should be rejected and there is evidence of lack of fit. The results of the model should be interpreted while taking this into account.

The discrimination, or predictive accuracy, of fixed effects model was assessed through a Receiver-Operating Characteristic (ROC) curve and through a

-2log(Likelihood) based Pseudo-$R^2$. The ROC curve showed low, but reasonable discrimination. The area under the curve was 0.67. Comparing the predicted to observed values, 67.2% were concordant and 32.8% were discordant. The pseudo-$R^2$ value was 5.83%, indicating a low proportion of the outcome variance explained.

The random effects model discrimination was similar to that of the fixed effects model. The area under the ROC curve was 0.66; indicating 66.4% of observed and predicted values were concordant while 33.6% were discordant. The pseudo-$R^2$ was 4.87%. A method to calculate the Hosmer-Lemeshow test of fit from a random effects model could not be found in the literature. While not a specific measure of fit, the analysis of the tract-level variance from a series of random effects models leading up to the final model provides some information concerning the fit of the model. This was done through fitting a series of models, starting with an empty model that partitioned the variance to between- and within-tract levels and then adding exposure, baseline, and finally the final set of individual factors. The 'empty model' partitioned 10.3% of the variance in preterm birth to the tract level and the remainder at the individual level. When mobility trajectories were added to the model the variation was reduced by only 5.56%. Adding the tract baseline deprivation explained 62.28% of the tract-level variance, reducing the tract-level variance to 3.89%. This indicates a strong association between baseline deprivation and tract preterm birth risk. Adding the individual-level factors to this model accounted for nearly all of the remaining tract level variance left only 2.25% of the variance at the tract-level and reducing the 'empty-model' variance by 78.20%. The median odds ratio reflected this step-wise reduction in tract-level variance as well, dropping from 1.36 in the empty model to 1.15 in the final model. The AIC was

progressively reduced through this series of models, indicating progressively better fit. (Table 6)

The marginal model discrimination was also similar to that of the fixed and random effects model. The area under the ROC curve was 0.66; indicating 65.99% of observed and predicted values were concordant while 34.01% were discordant. Again, a method to assess fit of GEE marginal models was not identified, so the fit was assumed to be similar to that of the fixed effects model.

*Comparison of Fixed and Random Effects Models*

The fixed and random effects conditional models have very similar structures but subtle differences. As has been discussed previously, the fixed effects model is considered the gold standard of the two since it makes fewer assumptions. The random effects model is more statistically efficient, though, and is expected to result in more precise parameter estimates. The closeness of the parameter estimates from each model and the difference in parameter precisions were jointly tested to determine whether the estimates provided by the random effects model are consistent with those of the fixed effects model through the Hausman test. The Hausman test was conducted comparing the final fixed effects model to the final random effects model. The test null hypothesis is that the two models are consistent. The test statistic is the ratio of the difference between random and fixed effects parameter estimates to the difference between the variance of these estimates, distributed on the chi-square distribution with degrees of freedom equal to the number of parameters compared under the null hypothesis. If the parameter

estimates were approximately equal, the numerator of the statistic would be small. If the variance of the random effects parameters were small relative to the variance of the fixed effects parameters, as is expected if both models are consistent since the random effects model is more efficient, then the test statistic would be expected to be small, resulting in failure to reject the null hypothesis that both models are consistent. If the null were rejected, the fixed effects model would be deemed consistent while the random effects model is not, leading to preference for the fixed effects model. If the null were not rejected and both models provided consistent estimation of associations, then due to the greater statistical efficiency of the random effects model, the random effects model would be the better model structure of the two. The test statistic is defined as W in equation 4.

$$W = [\beta_{FE} - \beta_{RE}]` [Var(\beta_{FE}) - Var(\beta_{RE})]^{-1} [\beta_{FE} - \beta_{RE}]$$

Equation 4. The Hausman test statistic. $[\beta_{FE} - \beta_{RE}]$ is the vector of differences in model parameter estimates between the fixed effects (FE) and random effects (RE) models and $[Var(\beta_{FE}) - Var(\beta_{RE})]^{-1}$ is the inverse of the matrix of differences in variances for each parameter. This produces a test statistic, W, that is distributed as chi-squared with degrees of freedom equal to the rank of the variance matrix under the null hypothesis of no difference between the models.

Although the parameter estimates were substantially similar, they were large relative to the variance differences, resulting in a denominator smaller than the numerator and therefore a large test statistic. The initial test statistic calculated was large but negative, which does not have a corresponding p-value on the chi-square distribution. The negative value of the test statistic was due to the generally smaller variance of the fixed effects parameters than the random effects. To find a p-value, the formula was revised, subtracting the fixed effects estimates and variances from the random effects.

This resulted, as expected, in the same test statistic but positive. The p-value from the chi-square distribution with 28 degrees of freedom, i.e. the rank of the variance matrix since 28 parameters were estimated by both models, was much less than 0.05, indicating the rejection of the null hypothesis that both models were consistent. This implies that the fixed effects model provided both more consistent and precise estimates than the random effects model. This was unexpected given the loss of precision predicted in the fixed effects model due to the excessive number of parameters estimated.

*Model Validity*

A primary threat to the validity of the model results was the potential lack of positivity. Positivity has been identified as one of three conditions necessary for causal inference from observational studies, along with exchangeability and well-defined interventions.[60] Positivity is the condition that all subjects have non-zero probability of each exposure group being compared. Since the probability of exposure is estimated by the set of non-exposure covariates, positivity can be described as the condition that all covariate patterns have non-zero probability of each exposure, i.e. that at least one individual within each covariate pattern experienced each exposure.

In this study, the positivity condition is that the probability that those experiencing each mobile exposure trajectory have an underlying non-zero probability of experiencing the non-mobile, or ‘stayer’ trajectory. Likewise, the non-mobile women that are compared to those with mobile trajectories must have non-zero probabilities of experiencing that trajectory. The concern for positivity first arose from the observation

that those living in certain baseline tracts were very unlikely to experience specific mobility trajectories. As an example, those living in the most deprived tract at baseline have, by definition, no probability of moving to a more deprived tract and therefore no probability of experiencing either of the downward mobility trajectories.

To quantify the extent of the problem related to trajectory probabilities in specific tracts, the proportion of individuals in each tract experiencing each trajectory was calculated. The problem was concentrated in the low baseline deprivation tracts where no individuals experienced the high upward mobility. Among mid-low baseline deprivation tracts there were also extremely few individuals experiencing the high upward mobility trajectory (average 0.0%). Positivity appeared to be less of a problem among high baseline deprivation tracts, where 8.7% of individuals, on average, experienced high downward mobility, in spite of having high baseline deprivation. This could be due to more tracts being in the high-deprivation tail of the baseline deprivation distribution than in the low-deprivation tail.

The average proportions presented here may hide the absolute number of tracts with zero individuals experiencing specific mobility trajectories. Furthermore, there may be specific covariate patterns within each tract that have no probability of specific mobility trajectories. This may be especially prevalent in tracts with few observations and is less likely to be a problem within tracts with larger numbers of observations. Therefore, excluding tracts with no members experiencing a given mobility trajectory may lead to systematic exclusion of less populated tracts or of tracts with few women having children, perhaps due to older age composition. Nevertheless, a propensity score analysis was conducted to assure positivity in the measures of association. The potential

bias arising from systematic exclusion of some tracts is a limitation that must be taken into account in interpretation of propensity score results.

The purpose of conducting a propensity score analysis is to account for non-positivity in the cohort. It is assumed that the estimated exposure probability is the same as the true underlying propensity, which may not be accurate if there are unmeasured or uncontrolled confounders. This propensity is estimated by the proportion of each covariate pattern that is exposed to a given exposure through regression of the exposure as the dependent variable on the set of independent variables identified in the final models. The analytic method used is to weight each subject in the model predicting preterm birth by the inverse of the probability of the observed exposure. That is, those who had a specific mobility trajectory receive weights equal to the inverse of the probability that a person with their set of covariates would experience that mobility trajectory while those with a non-mobile exposure trajectory, i.e. the referent group for all comparisons, receive weights equal to the inverse of the probability of the non-mobile trajectory. This method assures that non-positive individuals receive a weight of zero, and are therefore effectively excluded from the analysis. However, it does not account for the potential non-overlap of the propensity scores among exposed and unexposed subjects as a propensity score matched analysis would do, referred to as restricting to the area of common support.[61] A second analytic method was applied in which the subjects are weighted as in the first method, but instead of a conventional logistic regression of preterm birth on the weighted individual exposures, a fixed effects conditional logistic regression is conducted to ensure that those with mobile exposure trajectories are compared to stayers who shared the same baseline tract. This is similar to the ‘doubly

robust' techniques since it conditions on baseline tract both in estimating propensity scores and again in the exposure-outcome model. The technique is termed 'doubly robust' because it requires only that either the propensity score predicting model or the outcome predicting model is specified correctly, but not necessarily both.[61, 62] This dual control was not the purpose of including the baseline tract twice. Rather, it was included in the propensity score predicting model because baseline tract was significantly associated with mobility trajectories, as previously discussed. It was included again in the outcome predicting model not to control for tract again, but to ensure that within-tract estimates are calculated, making the proper comparison between the mobile exposure trajectories and stayers within the same baseline tract, a condition that was necessary for providing an answer the research question.

The individual propensities for each trajectory were estimated using fixed effects conditional regression with maternal baseline age, age-squared, education, race, prior preterm birth, inter-birth interval, and baseline tract as independent variables and each mobility trajectory modeled separately as the dependent variable. The distribution of probabilities by each observed trajectory was then examined. All observed mobility trajectories had non-zero probabilities of each other mobility trajectory. However, this does not imply that all individuals within each mobility trajectory had a non-zero probability. The positivity problem is apparent in the mobile trajectories. Among those with any mobile trajectory, the mean tract probability of being non-mobile, which is the referent group for comparisons, ranged from 0.08 to 0.10. This suggests that mobile individuals were relatively unlikely to be non-mobile. Among those with an observed

non-mobile trajectory there is less of a positivity problem as the mean probability of each mobile exposure trajectory is relatively large, ranging from 0.33 to 0.44. (Table 7)

The conclusions from the propensity score analyses were, in general, similar to the results of the traditional adjusted regression. Using the inverse propensity weighting technique, the OR among the high and intermediated upward mobility trajectories were not significant (High upward OR: 1.09 (95%CI 0.99, 1.21); Intermediate upward OR: 1.02 (0.93, 1.11)). Among those experiencing no change in deprivation the OR was 1.10 (1.02, 1.18). Those experiencing intermediate downward mobility had an OR of 1.10 (1.03, 1.16). The high downward mobility trajectory had an OR of 1.17 (1.07, 1.28). After conditioning on baseline tract through a fixed effects conditional model structure these estimates were shifted closer to the adjusted fixed-effects estimates but with wider confidence intervals. Odds ratios (95%CIs) for each trajectory were: high upward mobility 0.89 (0.81, 0.99), intermediate upward mobility 0.96 (0.88, 1.04), no change 1.09 (1.01, 1.10), intermediate downward mobility 1.11 (1.03, 1.20), and high downward mobility 1.17 (1.08, 1.28). In general, these estimates were further from the null than the traditionally adjusted fixed effects model. The percent of individuals excluded due to non-positivity in each mobility trajectory comparison to stayers were approximately equal: 11.15% in high upward, 10.94% in intermediate upward, 10.62% in no change, 10.57% in intermediate downward, and 10.55% in high downward. (Table 4)

It is unclear whether the propensity weighted model or the traditionally adjusted model provides a more accurate estimate. The traditional model may include individuals who violate positivity, with no probability of being in the high downward mobility trajectory due to their residence in very high deprivation baseline tracts. Since baseline

deprivation is associated with preterm birth, this could lead to a higher risk among the stayers and thus biasing the odds ratio towards the null. The propensity weighted model would exclude these tracts where the high downward mobility trajectory was not possible. However, it would also exclude tracts were the most increased trajectory was possible but was not actualized in any observed subjects. The predicted propensity score would violate positivity, but the actual propensity would not. However, there does not appear to be reason to believe the bias created by this exclusion would be differential with respect to preterm birth. A limitation of the propensity score modeling methods is that they do not take interactions into account, thus the estimates produced are averaged over all ages, inter-birth intervals, and baseline preterm birth statuses. This is likely responsible for a portion of the discrepancy between the traditional adjusted models and the propensity based models. Given the limitations of each method, there is no clear solution as to which provides the most accurate estimates. A stratified analysis by interaction terms through each model could produce comparable estimates, but this strategy was not pursued due to the approximate similarity between the estimates of the different techniques.

A second threat to model validity is the possibility of unmeasured confounding. Part of this could be due to underlying differences between women experiencing different mobility trajectories. Another part, not addressed here, could be due to trajectories of individual time-variant characteristics, such as income, that are associated with deprivation mobility trajectories and possibly with preterm birth. Underlying time-invariant differences between women experiencing mobile exposure trajectories and stayers can be addressed through an examination of the probability of preterm birth at

baseline based on mobility trajectories. If the individual preterm birth risk is actually changed by the mobility trajectory, then the probability of preterm birth prior to exposure should be approximately equal between the mobile and non-mobile prior to mobility. This was assessed indirectly through estimating the risk of the baseline birth being preterm based on the mobility trajectory experienced after baseline. This may yield some evidence as to whether risk was actually changed by the mobility trajectory or if the observed difference in follow-up preterm birth risk was due to underlying differences between movers with specific trajectories and stayers. The risk for baseline birth being preterm was assessed through the fixed effects model containing all of the covariates of the final follow-up birth preterm predicting fixed effects model. Baseline preterm birth was excluded as an independent variable since it is the dependent variable here. Only the high downward mobility trajectory was significantly associated with baseline birth being preterm birth, with an odds ratio of 1.08 (95%CI 1.03, 1.14). This can be compared to the OR for follow-up preterm birth of 1.11 (1.05, 1.17). The high upward mobility trajectory was not associated with baseline preterm birth (OR 1.01 (0.96, 1.06)) but was significantly associated with follow-up preterm birth (OR 0.93 (0.88, 0.98)). Similar results were found with the random effects and marginal models. This indicates that the probability of preterm birth at the follow-up birth prior to mobility may have been roughly equal between the mobile and non-mobile, which is further evidence of a causal association between moving to a lower deprivation tract and a decrease in preterm birth risk but also indicates that the association between downward mobility and subsequent preterm birth may be due in part to underlying differences between women who move to more deprived tracts and the non-mobile, within the same baseline tract. (Table 8)

## Discussion

In sum, our results show a consistent association of preterm birth risk with upward and downward mobility in exposure to neighborhood deprivation. Among individuals living in the same neighborhood at baseline, those who move to a higher deprivation neighborhood show an increase in risk for preterm birth while those who move to a lower deprivation neighborhood show a decrease in risk. The strengths of these associations are independent of the deprivation level of the baseline neighborhood. Furthermore, there is some evidence of a dose-response relationship between the degree of change in deprivation and the degree of change in preterm birth risk. Those with intermediate upward or downward mobility showed intermediate levels of change in preterm birth risk. Residential mobility itself was not the causal agent behind these associations, as those who moved to a new neighborhood but did not change levels of deprivation experienced no change in risk relative to those who did not move.

The magnitude of the increase in risk associated with high downward mobility was consistently greater than the magnitude of the decrease in risk associated with high upward mobility. The significance of the decrease in risk associated with upward mobility is questionable. While it was significant in the fixed effects crude and final models as well as the inverse probability of treatment model, it did not remain significant in the random effects or marginal final models. This pattern of significance remained when the risk differences and risk ratios were estimated using the marginal model.

Whether the difference in strength of the preterm birth association with high downward mobility compared to high upward mobility is due to an actual difference in

effect or a function of the distribution of deprivation change in this sample is not clear. The distribution of continuous deprivation change within each mobility group was not equivalent between groups and the mobility without deprivation change category was not centered exactly on zero change. This could have led to greater magnitudes of change among those coded as high downward mobility compared to the magnitudes of the highly upwardly mobile.

The association between upward or downward mobility and preterm birth risk was dependent on three main factors: maternal age at baseline, the length of the inter-birth interval, and whether or not the baseline birth was born preterm. The impact of upward mobility on preterm birth risk was greatest among women who were younger at baseline and had no significant association for women 30 years old at baseline and older. High downward mobility showed the opposite trend, with the impact increasing with age. If this is a true effect modification, then upward mobility only has an impact if this mobility takes place at a young age. Downward mobility, on the other hand, is not as detrimental among younger women but becomes increasingly detrimental with age. This could indicate that as exposure to deprivation accumulates with age, the cumulative impact on risk becomes more stable, changing less with the removal or lessening of deprivation exposure through upward mobility. However, moving downward has a greater impact as age increases, possibly indicating that moving to greater deprivation may have a greater impact among those with more accumulated exposure.

The interaction between inter-birth interval and upward or downward mobility was slightly more consistent than the interaction with age, although it was also less clearly linear. Both the impacts of upward and downward mobility were strongest among

those with short inter-birth intervals and decreased towards the null as the length of the interval increased. Based on considerations of the theorized mechanism linking deprivation exposure to preterm birth, it was expected that the change in risk following a move to greater or lesser deprivation would be gradual, leading to associations that became stronger with increasing time lived in the new neighborhood. However, this is the opposite as was observed, in so far as inter-birth interval can be interpreted as an indicator of time since residential mobility. However, due to the biological and social aspects of the association between inter-birth interval and preterm birth, interpreting the interval solely as a marker of time since mobility is not appropriate. Insight into how these mechanisms may interact with mobility is not apparent from the results of this study. Future studies should measure the time between mobility and child-birth more directly to better understand the relevance of the timing and duration of deprivation exposure.

Interestingly, there was no significant interaction between baseline deprivation and the impact of upward or downward mobility. The strength of the impact of upward or downward mobility was independent of the deprivation level of the baseline neighborhood. This implies that even among those in high baseline deprivation neighborhoods further downward mobility increases the risk of preterm birth in the same way as it would among those in mid or low deprivation baseline neighborhoods. Likewise, upward mobility is associated with a decrease in risk no matter whether the individual lives in a high deprivation neighborhood at baseline or a better-off neighborhood. It could be indicated from this that the impact of neighborhood deprivation follows a gradient rather than a threshold between deprived and not-deprived.

It also suggests that there is no leveling off of the impact of deprivation, as might be expected under a sigmoidal function of risk with deprivation: In high deprivation neighborhoods, moving to even greater deprivation increases preterm birth risk. In low deprivation neighborhoods, moving to even lower deprivation decreases risk.

*Strengths and Limitations*

In all, the mobility focused study design enabled us to provide evidence in support of a causal association between neighborhood deprivation and preterm birth in a way that has not been feasible in previous studies that relied on a single time-point measure of deprivation. These single time-point designs produce estimates that are likely confounded by individual differences between people who live in high deprivation neighborhoods and people who live in low deprivation neighborhoods. If there were sufficient overlap in these characteristics between neighborhood types and all confounding characteristics were measured then these estimates could be interpreted as causal. However, there is often little overlap in characteristics such as race between high and low deprivation neighborhoods. Furthermore, characteristics such as socioeconomic status are likely incompletely measured and some characteristics are likely not measured at all, especially when relying only on the information available from birth records for individual-level characteristics. Where these studies may have been biased by unmeasured confounding, our study reduces the potential bias by comparing individuals who share a baseline neighborhood.

An alternative to a causal interpretation of our results could be that those with high risk for preterm birth move to greater deprivation neighborhoods while those with low risk move to less deprived neighborhoods. This would support a selection explanation of the single-time point association between neighborhood deprivation and preterm birth rather than a causal explanation. However, there are several factors that lead us to believe our study supports evidence of a causal association rather than an association induced by neighborhood selection factors. The primary evidence against a selection process is the lack of association between baseline preterm birth and mobility in either direction. Those with high risk for preterm birth at second birth would be expected to have high risk for preterm birth at the baseline birth as well. If the heightened risk associated with downward mobility were due to underlying differences between the downwardly mobile and non-mobile, then it would be expected that downward mobility would be associated with baseline preterm birth. The null associations between mobility trajectories and baseline preterm birth suggest that the mobile were not intrinsically at different risk than the non-mobile. This is not to say the associations are necessarily due to a causal effect of change in deprivation, but rather that a general causal process is occurring between baseline and follow-up rather than only a selection process.

The main strengths of our study in terms of its ability to estimate causal associations are the reasonableness of its counterfactual assumption compared to neighborhood effects studies which measure neighborhood characteristics at a single time-point, its assessment of positivity, the robustness of estimates to a variety of analytic approaches, and its use of exposures defined in ways that may be more amenable to experimentation or intervention than the exposures in single time-point neighborhood

effects studies. The counterfactual assumption in this study is that the preterm birth outcomes of the non-mobile represent the outcomes that would have been experienced by the mobile if they had not moved. This is more reasonable than the assumption of single time-point studies that the birth outcomes experienced by those in high deprivation neighborhoods represent the outcomes that would have been experienced by those living in lower deprivation neighborhoods had they lived in the high deprivation neighborhoods.

Positivity was a concern in this study since there were some neighborhoods in which no individuals experienced some of the mobility trajectories. This non-positivity was addressed through inverse probability of treatment weighted models and the estimates were found to not substantially differ from the conventional regression estimates.

Furthermore, the final model estimates were robust to a variety of analytic approaches, including the marginal models using generalized estimating equations, the random effects conditional model which allowed an analysis of the between-neighborhood variation in preterm birth risk and the impact of baseline deprivation, and the fixed effects conditional model which provided the best control for neighborhood-level confounding by unmeasured characteristics of the baseline neighborhood.

Also, defining deprivation trajectories as exposures rather than neighborhood-level deprivation ensured that the exposures were measured at the individual level rather than the neighborhood level. Focusing on the change in deprivation allowed clear separation of the effects of deprivation change from the effects of the deprivation of the baseline neighborhood. Not only is this a methodological strength, it also increases the likelihood that our results could be verified by a realistic experiment. Neighborhood-level

exposures would require the randomization of neighborhoods to treatment or control in a hypothetical experiment. While this may be possible through a well-designed intervention that is able to change the deprivation level of neighborhoods without changing their composition, an individual-level intervention would be much easier to implement. For example, it is much easier to assign an individual to upward or downward residential mobility than it is to change the level of deprivation of a whole neighborhood.

In spite of these strengths, there are still a number of limitations to the causal interpretation of our estimates. Some of these are specific to this study while others are more general to studies of neighborhood effects. Specific to this study are the likelihood of remaining unmeasured confounding, possible misclassification of exposure, the indirect measurement of residential mobility, and failure to take pre-baseline deprivation trajectories into account. Limitations that are more general to neighborhood effects studies that were not addressed by this study are the use of census tract boundaries to approximate neighborhood boundaries and failure to acknowledge the spatial arrangement of neighborhoods and their inter-dependence.

While drawing comparisons between individuals sharing the same baseline neighborhood may have controlled many unmeasured confounders that would have biased a comparison between women living in different neighborhoods who had never shared a neighborhood, it does not control for all possible unmeasured confounding. Particularly, it does not control for individual characteristics that may be associated with upward or downward mobility or the neighborhood characteristics that change with an upward or downward change in neighborhood deprivation. The primary individual characteristic expected to confound the association between mobility and preterm birth is

socioeconomic status. We partially controlled for this using maternal education level and Medicaid payment for hospital costs at birth. However, these are inexact measures of SES and there is likely residual confounding. Furthermore, these measures of SES are not fine-grained enough to allow assessment of the change in SES between baseline and follow-up. It is likely that upward or downward mobility is associated with such a change, although the causal direction is likely not uniform. For example, an increase in income could lead to both decreased preterm birth risk and increased likelihood of upward residential mobility. It is also possible that upward residential mobility could lead to an increase in income through increased employment opportunities or other mechanisms. Whether or not these changes should be controlled for in the estimation of the total effect is unknown without more precise measurements. We did not control for any time-variant factors between baseline and follow-up. This includes neighborhood characteristics that may change with changes in deprivation, such as changes in crime rates and social cohesion. Even if we did measure neighborhood characteristics that change with moves to lower or higher deprivation, they could not be statistically controlled for due to lack of exposure to these changes among the non-mobile. They could be controlled for in comparisons of the upwardly or downwardly mobile and the mobile with no change in deprivation since both groups in this comparison would likely have some exposure to the confounding characteristic. Aside from confounding due to exposures occurring between time-points, there is also possible confounding by pre-baseline deprivation exposure. For example, the upwardly mobile may have experienced greater deprivation prior to baseline than the non-mobile depending on the time-line of their upward mobility. Likewise, the downwardly mobile may have experienced

decreased deprivation prior to baseline relative to the non-mobile. To some degree, we over-simplify in assuming that the pre-baseline deprivation exposures are uniform between movers and stayers.

Beyond confounding bias, there is a possibility of misclassification of the exposure. We relied on changes in census tract to indicate residential mobility. Due to the likely heterogeneity of area deprivation within census tracts, this could lead to some individuals who experience upward or downward mobility but remain within the census tract to be misclassified as non-movers. Likewise, those who move to neighborhoods with a different deprivation level may not have necessarily experienced a change in deprivation in their own exposure to deprivation, due to heterogeneity of environments within census tracts. Fundamentally, this concern is with the approximation of the neighborhood boundaries with census tract boundaries. If neighborhood boundaries were correctly measured, perhaps defined based on a radius around the individual residence, this misclassification would not be as much of a concern. Furthermore, in the interpretation of the association between change in deprivation through residential mobility and preterm birth, we assume that stayers do not substantially change deprivation exposure. While this was true for the majority of neighborhoods, based on the exploration of the continuously measured change in deprivation among stayers, it was not true in all neighborhoods. These neighborhoods undergoing substantial change in deprivation during the study could have been excluded from analyses to ensure less biased results, although this would have posed a problem for generalization.

A second concern with our measurement of upward and downward mobility is the inexact information on the timing of mobility between baseline and follow-up. This made

interpretation of the interaction between mobility and the length of the interval between baseline and follow-up difficult. Additionally, due to lack of information on specific moves, we assumed those who moved upward or downward did so in only one move. However, there may have been some individuals with multiple moves between birth and follow-up who experienced both increases and decreases in deprivation exposure throughout the interval or variations of the 'slope' of the mobility trajectory within the upwardly or downwardly mobile. Our classification based on two time-points may have resulted in some misclassification, but there does not seem to be strong reason to suspect this to be differential with respect to preterm birth.

*Comparison to Other Studies*

The findings of this study are similar to those found by the previous study using this same dataset that found cumulative exposure to deprivation was associated with increased risk of preterm birth.[51] The results of the former study are advanced by showing that the risk accumulated can be reduced when deprivation exposure is reduced and increased when deprivation exposure is increased. This suggests that a simple accumulation of risk with cumulative exposure model is not sufficient to explain how preterm birth risk is related to deprivation exposure throughout the life-course and that taking specific deprivation trajectories into account may also be necessary.

While the conclusions of this study are in agreement with the conclusions of many of the other studies of the relation between neighborhood deprivation and birth outcomes,

the design of this study and the questions it answers are unique, making quantitative comparisons to other studies difficult.

The measures of association that are made in cross-sectional studies compare women living in different neighborhoods who have never shared the same neighborhood. Since this study focuses instead on women who share a neighborhood at baseline but subsequently live in separate neighborhoods, the association between the deprivation trajectory and preterm birth is expected to be weaker than those found in cross-sectional studies. This expectation is based primarily on the idea that greater duration of exposure to a neighborhood environment leads to more pronounced impacts on health. Women who move to a new neighborhood between births are likely to have much less exposure to the destination neighborhood than the neighborhood measured at a single time point in a cross-sectional study.

As was discussed in the literature review, there have been several types of studies that have examined how changing or accumulating deprivation exposures throughout the life-course may be associated with birth outcomes. These offer more comparable estimates to those found in this study.

The first type of study identified an interaction between cross-sectionally measured maternal age and neighborhood deprivation and hypothesized that this could be due to an accumulation of risk, or from a more biologic perspective, an accumulation of stressor exposures resulting in chronic stress or weathering among the chronically exposed. The interaction between inter-birth interval length and deprivation mobility trajectory did not suggest that increased time in a new neighborhood environment resulted in increased impact on preterm birth risk. However, this could have been due to the imprecise relation

between inter-birth interval and duration of exposure to the new level of deprivation in combination with the underlying biological mechanism relating inter-birth interval to preterm birth risk.

The second study type came closer to more directly measuring duration of exposure to neighborhood environments by comparing immigrant and native-born women under the interpretation that exposure does not begin until the time of immigration for immigrant women. These studies found that among more recent immigrants neighborhood deprivation was not strongly associated with poor birth outcomes and that the strength of the association increased with increasing time since immigration. They did not measure pre-immigration neighborhood deprivation, limiting their comparability to the results of this study. However, the length of time since immigration necessary before the association between neighborhood deprivation and birth outcomes became significant was much longer than the average lengths of time between births in this study. The conclusions of this study, which suggest that preterm birth risk changes relatively soon after moving to a different level of deprivation exposure, much less than the 14 years identified in one of the immigration studies, are somewhat in disagreement with the immigration studies.[42] Furthermore, the tendency of decreasing impact of the deprivation trajectory with increasing inter-birth interval length is opposite from the tendency expected based on the immigration studies which suggest that the impact of a new level of deprivation exposure increases with increasing duration of the exposure.

Perhaps the study type with the most similar design to this study is that which attempted to measure lifetime deprivation mobility trajectories through inter-generationally linked birth records. This study uses the same technique of linking birth

records to create partial residential histories but focuses on a much shorter portion of the life-course: the time between births, rather than the time from birth to child-birth. A minor difference that results in differences in the interpretation of the trajectory associations is the method by which trajectories were defined. The inter-generational studies defined trajectories a priori, without regard to the observed residential mobility. The trajectories were defined by the quantile of deprivation at birth and the quantile of deprivation at child-birth. Thus, women could move upward from a first quartile neighborhood to a fourth quartile neighborhood or downward from fourth to first or any other combination. Consequently, the number of women in each category varied significantly as, for example, the first to fourth trajectory would be much less likely than the first to second trajectory. In this study, we defined deprivation trajectories based on the continuously measured change in deprivation observed in this cohort. The distribution of changes in deprivation among movers was then divided into quintiles that each corresponded to a different mobility trajectory, resulting in exposures that represent common experiences, rather than the experiences of only the few that experience more 'extreme' upward or downward mobility who may differ on other important characteristics that go unmeasured. Our method also has the benefit that the deprivation trajectories are defined independently of the baseline neighborhood deprivation, allowing the interaction between baseline deprivation and the deprivation trajectories to be assessed.

The measures of association found in one prototypical lifetime deprivation mobility study were similar in direction to those found in our study.[48] The risk ratio for decreasing two quartiles of deprivation was 0.8 and 0.6 for decreasing three quartiles. We

found a moderate decrease in deprivation to have an odds ratio of 0.96 ($p>0.05$) and a large decrease in deprivation to have an odds ratio of 0.89 ($p<0.05$) (IPTW Fixed Effects Model). These are in the same direction as the lifetime deprivation trajectory results but much smaller in magnitude. The difference is likely due in part to the shorter time-interval over which deprivation trajectories were measured and in part due to the different methods of defining trajectories between the two studies.

*Conclusions*

This study provides some evidence for a causal association between change in neighborhood deprivation through residential mobility and change in preterm birth risk and demonstrates the utility of an exposure trajectory focused longitudinal design in evaluating the potential causality of a neighborhood characteristic. Returning to our study objective, to examine the association between movement to lower or higher deprivation neighborhoods and risk for preterm birth relative to the non-mobile, we found that among women sharing a baseline neighborhood, those who moved to lower deprivation neighborhoods had a lower risk for subsequent preterm birth than women staying in the baseline neighborhood. Those who moved to higher deprivation neighborhoods were at greater risk. The magnitudes of the associations were small, but significant. These associations were likely not entirely due to individual differences between the upwardly and downwardly mobile and the non-mobile since the risk for preterm birth at baseline did not differ between the mobile and non-mobile. This is evidence of a causal process taking place between baseline and follow-up that produces the observed differences in

preterm birth risk. That the magnitude of the association between upward or downward mobility depended on the magnitude of deprivation change, as seen in the differences between those with intermediate and high mobility, suggests that neighborhood deprivation is involved in this causal process. Finally, we found evidence that the impact of mobility on preterm birth depended on maternal age at baseline and the time between baseline and follow-up, but not on the degree of baseline deprivation. The dependence on maternal age can be interpreted shows the importance of the timing of mobility in the life-course to its impact on health. The dependence on the inter-birth length provides some evidence that the impact of mobility changes with the time since mobility, although our data did not allow a more concrete interpretation due to the imprecision of our mobility measurements. That the associations between mobility and preterm birth risk did not depend on the baseline deprivation level provides some insight into the structure of the relation between deprivation and preterm birth, suggesting a linear association between continuous deprivation and risk rather than a threshold or sigmoidal association.

In sum, our results provide some evidence for a causal association between exposure to neighborhood deprivation during the years immediately prior to child-birth and preterm birth. Furthermore, these conclusions suggest that interventions aimed at helping women living in deprived areas move to areas of less deprivation or aimed at helping women avoid moving to greater deprivation areas may prevent preterm births. The effect of mobility to more or less deprived areas was found to be independent of baseline deprivation, suggesting that interventions would be effective in all neighborhood settings, not only in helping those in high deprivation move to less deprived areas but also in helping those in moderate deprivation move to lower deprivation. Likewise,

preventing downward mobility may have an effect on all people, regardless of current levels of deprivation.

*Public Health Impact and Future Directions*

While the parameter estimates from our study provide some evidence for a change in preterm birth risk following a residential move to a more or less deprived neighborhood, the public health impact of our study is primarily in its demonstration of a longitudinal study design that can produce a more complex and adequate explanation of the association between characteristics of the neighborhood environment and individual health outcomes than has been available from studies reliant on single time-point measures of the neighborhood. The strengths of our design in evaluating the causality of an association between neighborhood characteristics and individual outcomes have been reviewed at length. Beyond this, our design provides a conceptualization of neighborhood effects more in line with current theory, particularly the ecosocial theory. The ecosocial theory emphasizes that characteristics of the environments lived in throughout the life course cause individual health outcomes through many processes of embodiment that take place over time and may differ at different times during the life-course.[10-12] This leads to a concern that explanations of associations of neighborhood characteristics with health outcomes are incomplete without containing elements of exposure timing and duration, in the context of the life-course of the exposed. Timing is emphasized in the context of the life-course to distinguish this aspect of timing from conceptualizations that emphasize only the timing of an event prior to an outcome. Here, timing could include

the age or life-stage of the individual when exposed, recognizing that exposure during certain critical periods such as early life or during pregnancy could operate differently than exposure at other times during the life-course. In our study, timing was emphasized by separating exposure in the years immediately prior to child-birth from exposures during the previous life-course through comparisons of individuals with a shared baseline neighborhood. While longitudinal data allow explanations that account for exposure timing, they do not offer a clear way to assess the duration of exposure without also focusing on residential mobility. By doing so, we were able to identify changes in exposure within individuals and thereby estimate the duration of post-change exposure. However, our reliance on birth records and census data did not allow us to measure residential mobility directly, limiting our conclusions regarding exposure duration. Future longitudinal studies that use residential mobility to assess neighborhood effects should more precisely measure the timing of mobility in order to better assess duration of exposure to the new neighborhood.

A better understanding of how when an exposure to a neighborhood characteristic occurs and for how long an individual is exposed may lead to more effective public health interventions. For example, programs that provide assistance in residential mobility out of deprived areas could be constructed that take individual life-course, including prior exposures, into account in prioritizing individuals who would be expected to experience a decrease in health risk following the move. Additionally, and perhaps more realistically, this design could guide further research toward examining the portion of the life-course during which exposures to neighborhood characteristics have the most impact, leading to better identification of causal mechanisms that could be intervened on.

For example, the results of our study suggest that the relevant timing of exposure to neighborhood deprivation is not solely during pregnancy or the years immediately preceding pregnancy, but that some mechanism does operate during this time linking deprivation mobility to change in preterm birth risk. This is in accord with the models of chronic stress and preterm birth that suggest that exposures throughout the life-course jointly impact preterm birth risk. It would be in opposition to a hypothetical model that posited that women who live in high deprivation neighborhoods are at increased risk for a particular exposure, such as a high stress inducing event, during pregnancy that causes preterm birth.

Future studies using our design are encouraged to more directly measure residential mobility, including when the move occurs and whether more than one move occurs. Additionally, better measures of individual SES and how it changes with residential mobility should be used in studies which examine socioeconomic characteristics of neighborhoods as this likely produced unmeasured confounding bias in our study. With better measurements, our design offers a valuable a new approach to the study of neighborhood effects. This approach has strengths over single time-point studies including in assessing evidence of causality, in promoting life-course conceptualizations of how neighborhood characteristics may result in health outcomes, and in producing estimates that are verifiable by possible experimental studies. Nevertheless, there is also a need for this approach to be scrutinized further from both methodological and public health intervention perspectives.

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**Table 1. Distribution of mobility trajectories and preterm birth at follow-up by covariates in the full cohort.**

| | Number of Women (n=170,865) | | Follow-Up Preterm Births (n=17324) | | Neighborhood Deprivation Exposure Trajectory | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Non-Mobile | Mobile Trajectories | | | | | |
| | N | % | Prevalence % | Odds Ratio (95% CI) | % (n=80321) | High Upward % (n=18109) | Intermediate Upward % (n=18109) | No Change % (n=18108) | Intermediate Downward % (n=18110) | High Downward % (n=18108) | ANOVA p-value |
| *Follow-Up Preterm Birth* | | | | | | | | | | | |
| Preterm | 17,324 | 10.1 | 10.1 | -- | 9.4 | 11.6 | 10.4 | 9.5 | 10.3 | 9.4 | <0.01 |
| Term | 153,541 | 89.9 | 89.9 | -- | 90.6 | 88.4 | 89.6 | 90.5 | 89.7 | 90.6 | |
| *Baseline Neighborhood Deprivation Quintile* | | | | | | | | | | | |
| Q1 (least deprived) | 34,170 | 20.0 | 7.4 | ref | 27.1 | 0.0 | 0.5 | 20.2 | 28.1 | 19.9 | <0.01 |
| Q2 | 34,160 | 20.0 | 8.6 | 1.19 (1.11, 1.26) | 23.1 | 0.0 | 13.5 | 26.8 | 23.3 | 22.6 | |
| Q3 | 34,193 | 20.0 | 9.8 | 1.37 (1.29, 1.46) | 19.2 | 4.5 | 31.2 | 21.2 | 20.9 | 25.7 | |
| Q4 | 34,170 | 20.0 | 11.1 | 1.57 (1.47, 1.68) | 15.7 | 29.3 | 33.3 | 20.6 | 18.7 | 17.1 | |
| Q5 (most deprived) | 34,172 | 20.0 | 13.9 | 2.03 (1.89, 2.18) | 14.9 | 66.2 | 21.5 | 11.1 | 9.0 | 14.7 | |
| *Maternal Age at Baseline, years* | | | | | | | | | | | |
| <15 | 947 | 0.6 | 16.5 | 1.40 (1.17, 1.69) | 0.4 | 0.5 | 0.5 | 0.5 | 0.6 | 1.1 | <0.01 |
| 15-19 | 27,037 | 15.8 | 13.2 | 1.22 (1.16, 1.29) | 10.7 | 16.5 | 16.5 | 14.6 | 18.1 | 29.0 | |
| 20-24 | 39,063 | 22.9 | 10.8 | 1.07 (1.02, 1.13) | 16.4 | 27.5 | 27.5 | 24.8 | 28.0 | 32.0 | |
| 25-29 | 51,284 | 30.0 | 9.0 | ref | 31.5 | 31.2 | 31.2 | 32.8 | 30.4 | 23.0 | |
| 30-34 | 41,146 | 24.1 | 8.7 | 1.03 (0.98, 1.08) | 31.6 | 19.7 | 19.7 | 22.0 | 18.6 | 11.9 | |
| 35-39 | 10,625 | 6.2 | 10.2 | 1.23 (1.14, 1.32) | 8.8 | 4.3 | 4.3 | 5.0 | 4.1 | 2.9 | |
| 40+ | 763 | 0.5 | 9.8 | 1.17 (0.92, 1.48) | 0.7 | 0.3 | 0.3 | 0.3 | 0.3 | 0.2 | |
| *Inter-birth Interval, years* | | | | | | | | | | | |
| < 1 | 329 | 0.2 | 37.4 | 5.39 (4.30, 6.74) | 0.2 | 0.1 | 0.1 | 0.1 | 0.1 | 0.4 | <0.01 |
| 1-2 | 83,575 | 48.9 | 10.5 | 1.19 (1.14, 1.23) | 57.8 | 36.2 | 39.1 | 40.5 | 43.2 | 46.2 | |
| 3-4 | 59,501 | 34.8 | 8.9 | ref | 33.1 | 34.6 | 37.5 | 38.5 | 36.8 | 34.6 | |
| 5-6 | 18,702 | 11.0 | 10.7 | 1.14 (1.08, 1.20) | 6.9 | 17.7 | 15.0 | 13.9 | 13.1 | 12.9 | |
| 7+ | 8,760 | 5.1 | 12.9 | 1.34 (1.25, 1.42) | 2.0 | 11.4 | 8.3 | 7.0 | 6.8 | 5.9 | |
| *Maternal Race* | | | | | | | | | | | |
| White | 101,042 | 63.7 | 7.9 | ref | 70.8 | 42.8 | 59.7 | 69.3 | 67.3 | 47.5 | <0.01 |
| Black | 57,560 | 36.3 | 14.2 | 1.63 (1.55, 1.72) | 29.2 | 57.2 | 40.3 | 30.7 | 32.7 | 52.5 | |
| Other / Missing | 12,263 | | | | | | | | | | |
| *Maternal Education* | | | | | | | | | | | |
| <9th grade | 9,521 | 5.8 | 11.3 | 1.27 (1.18, 1.38) | 4.6 | 8.5 | 5.9 | 5.2 | 5.7 | 8.4 | <0.01 |
| 9th-11th grade | 25,194 | 15.2 | 13.6 | 1.38 (1.31, 1.45) | 10.6 | 23.7 | 15.8 | 13.1 | 17.0 | 27.0 | |
| High School / GED | 39,545 | 23.9 | 11.8 | 1.26 (1.21, 1.31) | 19.8 | 29.4 | 26.4 | 23.9 | 26.8 | 31.0 | |
| At least some college | 91,418 | 55.2 | 8.3 | ref | 65.0 | 38.4 | 52.0 | 57.8 | 50.5 | 33.6 | |
| Missing | 5,187 | | | | | | | | | | |

**Table 1 continued. Distribution of Mobility Trajectories and Preterm Birth by Covariates in the Full Cohort**

| | Number of Women (n=170,865) | | Follow-Up Preterm Births (n=17324) | | Neighborhood Deprivation Exposure Trajectory | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Non-Mobile | Mobile Trajectories | | | | | |
| | N | % | Prevalence % | Odds Ratio (95% CI) | % (n=80321) | High Upward % (n=18109) | Intermediate Upward % (n=18109) | No Change % (n=18108) | Intermediate Downward % (n=18110) | High Downward % (n=18108) | ANOVA p-value |
| *Payer at Baseline* | | | | | | | | | | | |
| Medicaid | 59,310 | 34.7 | 12.6 | 1.21 (1.16, 1.26) | 24.2 | 53.2 | 39.0 | 33.1 | 39.2 | 55.6 | <0.01 |
| Other | 111,555 | 65.3 | 8.8 | ref | 75.8 | 46.8 | 61.0 | 66.9 | 60.8 | 44.4 | |
| *Parity at Baseline* | | | | | | | | | | | |
| 1st Birth | 125,288 | 74.0 | 9.4 | ref | 75.9 | 69.0 | 73.7 | 75.2 | 73.9 | 70.4 | <0.01 |
| 2nd Birth | 28,257 | 16.7 | 11.1 | 1.14 (1.10, 1.19) | 15.6 | 19.1 | 17.3 | 16.6 | 17.3 | 18.2 | |
| 3rd Birth | 10,061 | 6.0 | 12.3 | 1.23 (1.15, 1.31) | 5.6 | 7.2 | 6.0 | 5.5 | 5.8 | 6.8 | |
| 4th or Higher | 5,565 | 3.3 | 16.3 | 1.58 (1.46, 1.72) | 3.0 | 4.8 | 3.0 | 2.8 | 3.0 | 4.5 | |
| Missing | 1,694 | | | | | | | | | | |
| *Marital Status, Baseline* | | | | | | | | | | | |
| Married | 11,975 | 69.1 | 8.3 | 0.68 (0.65, 0.71) | 78.7 | 50.5 | 66.4 | 72.0 | 66.5 | 47.3 | <0.01 |
| Unmarried | 52,887 | 30.9 | 14.2 | ref | 21.4 | 49.5 | 33.6 | 28.0 | 33.5 | 53.7 | |
| Missing | 3 | | | | | | | | | | |
| *Alcohol use during 1st Pregnancy* | | | | | | | | | | | |
| Yes | 1,515 | 0.9 | 14.3 | 1.49 (1.28, 1.73) | 1.0 | 0.9 | 0.7 | 0.9 | 0.7 | 1.0 | 0.02 |
| No | 168,563 | 99.1 | 10.1 | ref | 99.0 | 99.1 | 99.3 | 99.1 | 99.3 | 99.0 | |
| Missing | 787 | | | | | | | | | | |
| *Tobacco use during 1st Pregnancy* | | | | | | | | | | | |
| Yes | 7,619 | 4.5 | 15.0 | 1.51 (1.41, 1.62) | 3.2 | 5.2 | 4.7 | 4.8 | 6.1 | 7.0 | <0.01 |
| No | 162,475 | 95.5 | 9.9 | ref | 96.8 | 94.8 | 95.3 | 95.2 | 93.9 | 93.0 | |
| Missing | 771 | | | | | | | | | | |
| *Adequacy of Prenatal Care (Kotelchuck index), Baseline* | | | | | | | | | | | |
| Inadequate | 12,839 | 7.8 | 13.7 | 1.55 (1.46, 1.65) | 6.0 | 11.3 | 8.0 | 7.1 | 8.1 | 12.2 | <0.01 |
| Intermediate | 16,744 | 10.1 | 8.3 | 1.00 (0.94, 1.07) | 9.7 | 11.2 | 10.2 | 10.1 | 10.0 | 10.8 | |
| Adequate | 82,605 | 49.9 | 8.0 | ref | 51.6 | 46.0 | 49.8 | 50.5 | 49.9 | 45.8 | |
| Adequate plus | 63,284 | 32.2 | 12.9 | 1.67 (1.61, 1.73) | 32.7 | 31.6 | 32.0 | 32.2 | 32.0 | 31.2 | |
| Missing | 5,393 | | | | | | | | | | |
| *Baseline Birth Preterm* | | | | | | | | | | | |
| Preterm | 16,715 | 9.8 | 26.1 | 3.68 (3.51, 3.83) | 9.3 | 11.0 | 9.7 | 9.3 | 9.8 | 11.3 | <0.01 |
| Term | 154,150 | 90.2 | 8.4 | ref | 90.7 | 89.0 | 90.3 | 90.7 | 90.3 | 88.7 | |

**Table 2A. Average Tract Follow-up Preterm Birth Prevalence by Baseline Deprivation Quintile, Mean (95% CI)**

| | |
|---|---|
| High Deprivation | 13.9% (12.8%, 15.1%) |
| Mid-High | 11.3% (10.4%, 12.3%) |
| Mid | 9.8% (9.0%, 10.6%) |
| Mid-Low | 8.4% (7.8%, 9.1%) |
| Low Deprivation | 7.3% (6.7%, 7.9%) |

**Table 2B. Tract Stratified Approach: Average within-tract associations between mobility trajectories and preterm birth**

| Mobility Trajectory | Avg. Risk[a] (SD) | Avg. RD[b] (SD) | Avg. RR[b] (SD) |
|---|---|---|---|
| High Upward | 12.74% (11.80%) | -1.77% (11.26%) | 0.98 (1.07) |
| Intermediate Upward | 13.63% (19.82%) | 0.89% (18.92%) | 1.20 (2.19) |
| No Change | 14.24% (19.90%) | 2.53% (18.86%) | 1.35 (1.67) |
| Intermediate Downward | 13.76% (14.50%) | 2.18% (13.69%) | 1.30 (1.34) |
| High Downward | 16.27% (17.07%) | 4.30% (16.31%) | 1.59 (1.82) |
| Non-Mobile | 11.86% (6.42%) | ref | ref |

[a] The risk for follow-up preterm birth was estimated within each trajectory within each tract and averaged across all tracts.

[b] The risk difference and risk ratio between each mobile trajectory and the non-mobile trajectory was estimated within each tract and these were then averaged across all tracts.

**Table 3. Summary of Tract-Level Characteristics**

| | Mean (SD)[a] | Min | Max |
|---|---|---|---|
| *N per Tract* | 304 (193) | 20 | 1534 |
| *Preterm Prevalence* | 10.6% (3.9%) | 1.4% | 30.9% |
| *Mobility Trajectory Prevalence* | | | |
| %High Upward | 12.0% (16.7%) | 0.0% | 78.7% |
| %Intermediate Upward | 9.8% (8.0%) | 0.0% | 34.9% |
| %No Change | 10.1% (5.2%) | 0.0% | 30.2% |
| %ntermediate Downward | 10.2% (5.2%) | 0.0% | 30.5% |
| %High Downward | 11.3% (7.1%) | 0.2% | 47.6% |
| *Non-Mobile Prevalence* | 46.6% (14.8%) | 9.3% | 83.5% |
| *Baseline Deprivation*[b] | -0.32 (1.12) | -1.69 | 4.44 |
| *Covariate Clustering* | | | |
| *Maternal Age at Baseline (years)* | 26.0 (2.8) | 20.1 | 32.1 |
| *Inter-birth Interval (years)* | 3.0 (0.2) | 2.3 | 3.8 |
| *Maternal Race Prevalence* | | | |
| %Black | 36.8% (34.6%) | 0.0% | 100.0% |
| %White | 56.6% (33.4%) | 0.0% | 99.6% |
| %Other | 6.5% (5.3%) | 0.0% | 29.8% |
| *Maternal Education Prevalence* | | | |
| %<9th grade | 5.2% (5.7%) | 0.0% | 49.0% |
| %9th-11th grade | 16.2% (12.8%) | 0.0% | 60.3% |
| %High School / GED | 23.5% (10.5%) | 1.5% | 48.2% |
| %At least some college | 52.3% (24.0%) | 3.9% | 95.9% |
| %Unknown | 2.8% (2.1%) | 0.0% | 18.0% |
| *%Medicaid Payment at 1st Birth* | 36.5% (22.9%) | 0.70% | 91.90% |
| *%Marrried* | 66.1% (26.5%) | 3.30% | 100% |
| *%Alcohol use during 1st pregnancy* | 1.0% (1.1%) | 0.00% | 7.50% |
| *%Tobacco use during 1st pregnancy* | 4.9% (3.6%) | 0.00% | 21.80% |
| *Prenatal Care Adequacy* | | | |
| %Inadequate | 8.0% (5.7%) | 0.00% | 28.80% |
| %Intermediate | 9.8% (2.9%) | 2.10% | 20.10% |
| %Adequate | 47.3% (8.0%) | 17.80% | 70.00% |
| %Adequate plus | 31.5% (4.9%) | 15.00% | 46.80% |
| *Baseline Birth Preterm* | 10.1% (3.2%) | 1.80% | 28.20% |

[a] The prevalence of categorical variables and the mean of continuous variables was calculated within each tract. The mean and standard deviation reported here is that of this distribution of tract means or proportions. The minimum and maximum values are reported as they suggest a lack of positivity due to the absence of some mobility trajectories and of some covariates in some neighborhoods. This is taken into account in the Inverse Probability of Treatment Weighted analysis.

[b] Tract deprivation, measured by NDI, in 2000

**Table 4. Regression modeling results of the association between deprivation mobility trajectories and subsequent preterm birth.**

| | Marginal Model[a] | | Random Effects Conditional Model[b] | | Fixed Effects Conditional Model[c] | | IPTW Model[d] | |
|---|---|---|---|---|---|---|---|---|
| | Crude[e] | Fully Adjusted[f] | Crude[e] | Fully Adjusted[f] | Crude | Fully Adjusted[f] | Conventional | Fixed Effects |
| **Mobility Trajectory** | **OR (95% CI)** | **OR (95% CI)** | **OR (95% CI)** | **OR (95% CI)** | **OR (95% CI)** | **OR (95% CI)** | **OR (95% CI)** | **OR (95% CI)** |
| High Upward | 0.90 (0.85, 0.95) | 1.01 (0.94, 1.08) | 0.90 (0.85, 0.95) | 1.01 (0.94, 1.08) | 0.84 (0.80, 0.88) | 0.93 (0.88, 0.98) | 1.09 (0.99, 1.21) | 0.89 (0.81, 0.99) |
| Intermediate Upward | 0.98 (0.93, 1.04) | 1.04 (0.97, 1.11) | 0.98 (0.93, 1.04) | 1.04 (0.97, 1.11) | 0.95 (0.91, 1.00) | 0.98 (0.93, 1.04) | 1.02 (0.93, 1.11) | 0.96 (0.88, 1.04) |
| No Change | 1.02 (0.96, 1.08) | 1.06 (0.99, 1.13) | 1.02 (0.96, 1.07) | 1.06 (0.99, 1.13) | 0.98 (0.93, 1.03) | 1.00 (0.94, 1.06) | 1.10 (1.02, 1.18) | 1.09 (1.01, 1.10) |
| Intermediate Downward | 1.16 (1.09, 1.22) | 1.10 (1.03, 1.18) | 1.14 (1.08, 1.20) | 1.10 (1.03, 1.18) | 1.09 (1.04, 1.15) | 1.04 (0.98, 1.09) | 1.10 (1.03, 1.16) | 1.11 (1.03, 1.20) |
| High Downward | 1.32 (1.25, 1.39) | 1.21 (1.14, 1.30) | 1.30 (1.24, 1.37) | 1.21 (1.13, 1.30) | 1.22 (1.17, 1.27) | 1.15 (1.09, 1.21) | 1.17 (1.07, 1.28) | 1.17 (1.08, 1.28) |
| Non-Mobile | ref | ref | ref | ref | ref | ref | ref | ref |

[a] The marginal models were fit using generalized estimating equations in SAS's Proc Genmood, using the Repeated statement to specify and account for clustering within tracts.

[b] The random effects conditional models were fit using maximum likelihood estimation in SAS's Proc Glimmix with a random intercept specified for each tract and a compound symmetric covariance structure.

[c] Fixed effect conditional models were fit using a dummy variable approach through which an intercept parameter is estimated for each tract. SAS's Proc SurveyLogistic was used with tract clustering specified.

[d] The Inverse Probability of Treatment Weighted (IPTW) models were fit using weights calculated from trajectory propensities estimated through SAS's Proc SurveyLogistic. The conventional IPTW model uses these weights and Proc SurveyLogistic with tract clustering specified. The fixed effects IPTW model uses these weights and also estimates tract intercepts through a dummy variable approach to ensure comparisons are made within-tracts. The purpose of the IPTW approach is to account for potential non-positivity in other approaches.

[e] Adjusted for baseline neighbhorhood deprivation for consistency of crude estimates with fixed effects model crude estimates.

[f] Fully adjusted models are adjusted for maternal race, education, baseline preterm birth, age at baseline, and inter-birth interval length and set to mean values of interaction terms ( Age=26 years, No baseline preterm birth, 3 year inter-birth interval). These were identified from a modeling process that began from a model with many more variables and excluded those that did not interact with or substantially confound the individual mobility trajectory associations with preterm birth.

OR (95% CI): Odds ratio (95% Confidence Interval)

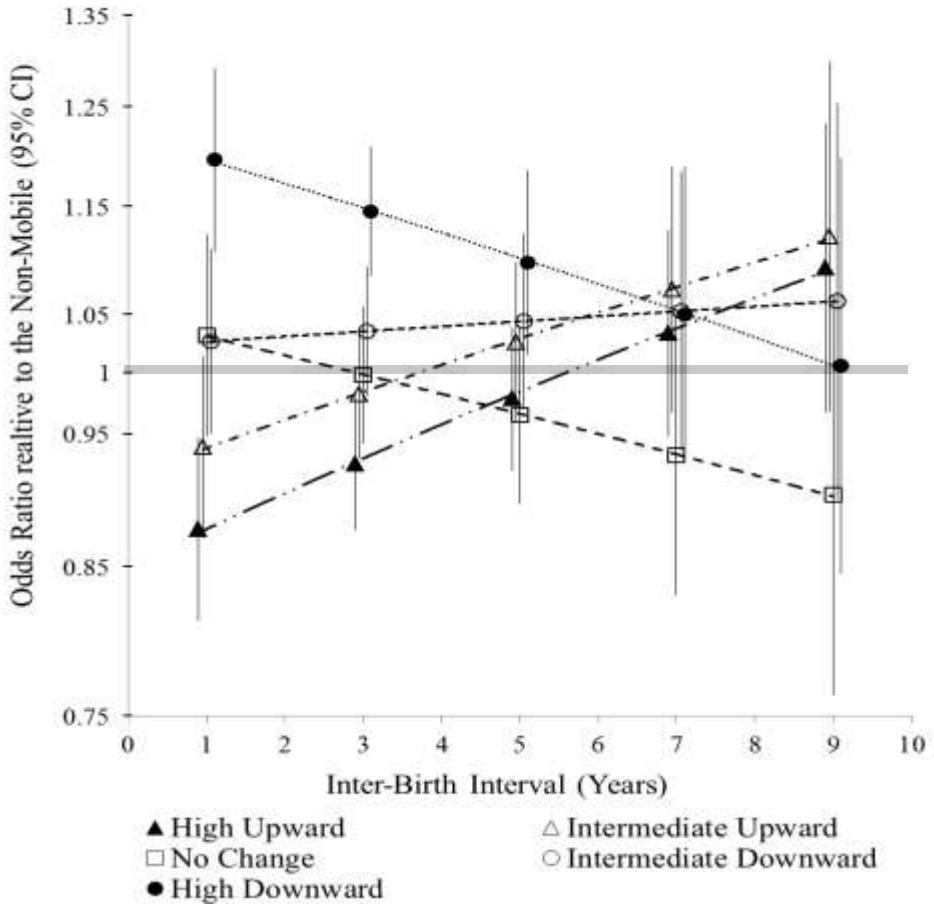


Figure 4. Linear Inter-Birth Interval Interaction with the Association between Mobility Trajectory and Preterm Birth. Estimates are from the final adjusted fixed effects conditional model. Associations between mobility trajectories and preterm birth appear strongest at shorter inter-birth intervals. A linear interaction is assumed both here and in the final model.

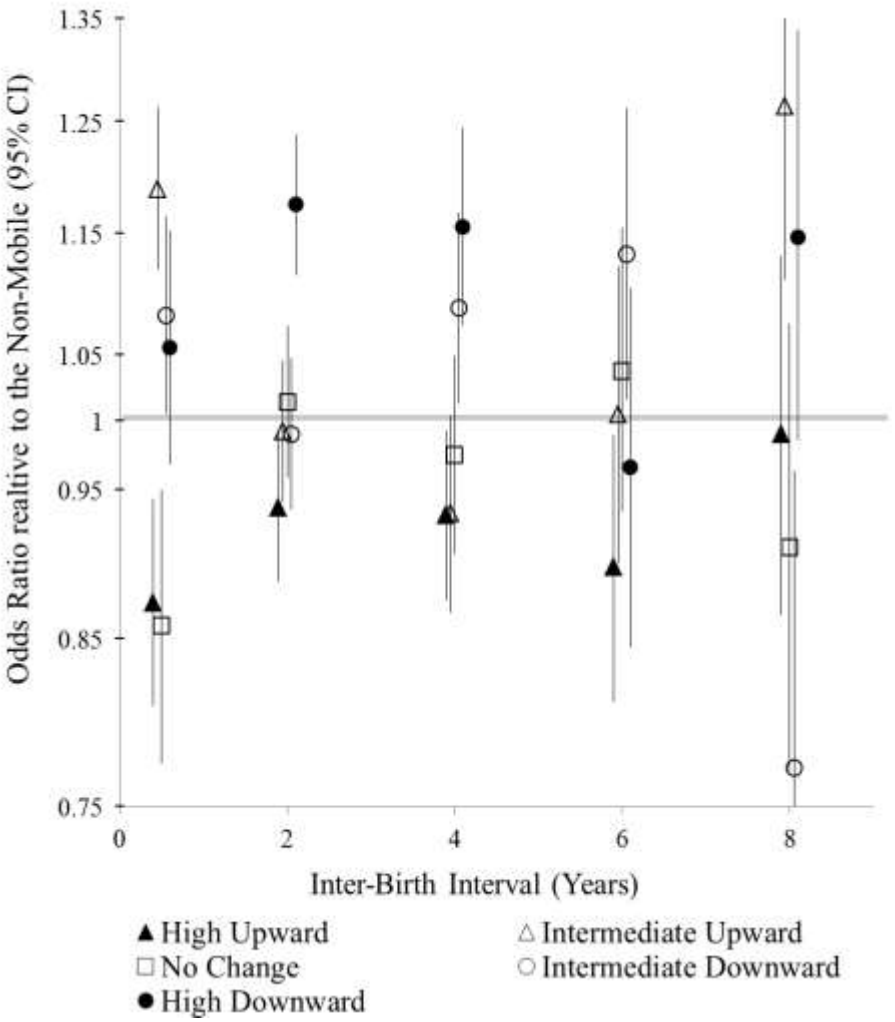


Figure 5. Categorical Inter-Birth Interval Interaction with the Association between Mobility Trajectory and Preterm Birth. Two-year inter-birth interval categories were fit in the final fixed effects conditional model to evaluate the assumption of a linear interaction. Some clear deviations from linearity are noticeable, but no other trend is apparent.

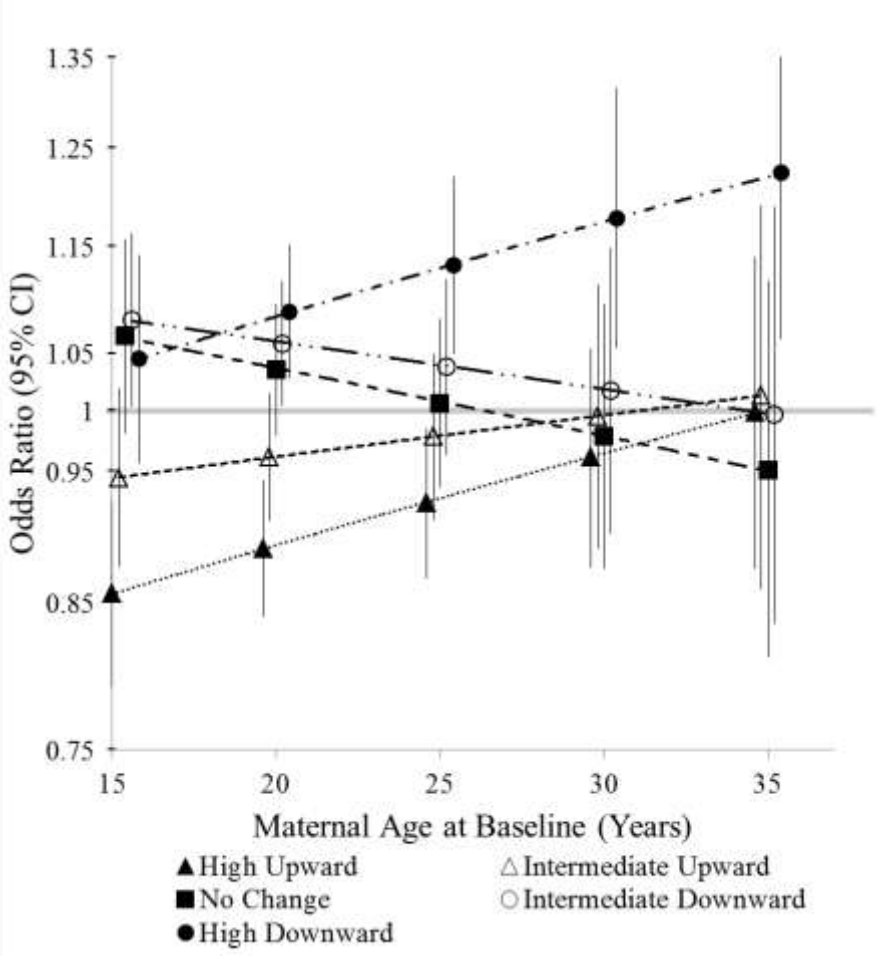


Figure 6. Change in the Association of Mobility Trajectory and Preterm Birth by Maternal Age. The interaction between maternal age at baseline and mobility trajectory from the final fixed effects conditional model estimates showed a general reduction in the magnitude of the trajectory association with preterm birth as age increased. The high downward mobility trajectory does not follow this pattern. The interactions between age and mobility trajectories are assumed to be linear. Quadratic interactions were fit but did not vary substantially from linearity.

**Table 5. Interaction between mobility trajectories and baseline preterm birth: Stratified measures of association.**

| | Fully Adjusted Fixed Effects Model Odds Ratios | | Fully Adjusted Marginal Model Risk Differences | |
|---|---|---|---|---|
| | Preterm | Term | Preterm | Term |
| **Mobility Trajectory** | **OR (95% CI)** | **OR (95% CI)** | **RD (95% CI)** | **RD (95% CI)** |
| High Upward | 0.85 (0.78, 0.94) | 0.93 (0.88, 0.98) | -1.09% (-3.26%, 1.88%) | -0.43% (-1.01%, 0.15%) |
| Intermediate Upward | 0.99 (0.89, 1.10) | 0.98 (0.93, 1.04) | -0.13% (-2.53%, 2.28%) | 0.03% (-0.47%, 0.53%) |
| No Change | 0.94 (0.84, 1.05) | 1.00 (0.94, 1.06) | -2.17% (-4.58%, 0.23%) | 0.30% (-0.18%, 0.77%) |
| Intermediate Downward | 1.15 (1.04, 1.27) | 1.04 (0.98, 1.09) | 1.87% (-0.43%, 4.18%) | 0.64% (0.16%, 1.11%) |
| High Downward | 1.08 (0.98, 1.18) | 1.15 (1.09, 1.21) | 1.88% (-0.38%, 4.14%) | 1.30% (0.73%, 1.88%) |
| Non-Mobile | ref | ref | ref | ref |

**Table 6. Random Intercept Model: Measures of tract-level variation and association with mobility trajectories of follow-up preterm birth**

| | Empty Model | Crude Model | Baseline Deprivation Adjusted Model | Final Model[a] |
|---|---|---|---|---|
| **Measures of Association (OR, 95% CI)** | | | | |
| Mobility Trajectory | | | | |
| High Upward | -- | 1.00 (0.94, 1.06) | 0.90 (0.85, 0.95) | 1.01 (0.94, 1.08) |
| Intermediate Upward | -- | 1.04 (0.98, 1.10) | 0.98 (0.93, 1.04) | 1.04 (0.97, 1.11) |
| No Change | -- | 1.02 (0.97, 1.08) | 1.02 (0.96, 1.07) | 1.06 (0.99, 1.13) |
| Intermediate Downward | -- | 1.13 (1.07, 1.19) | 1.14 (1.08, 1.20) | 1.10 (1.03, 1.18) |
| High Downward | -- | 1.23 (1.23, 1.36) | 1.30 (1.24, 1.37) | 1.21 (1.13, 1.30) |
| Non-Mobile | -- | ref | ref | ref |
| **Measures of Variation** | | | | |
| Neighborhood intercept variance (SE) | 0.103 (0.009) | 0.097 (0.009) | 0.039 (0.004 ) | 0.022 (0.003) |
| PCV | -- | -5.56% | -62.28% | -78.20% |
| MOR | 1.36 | 1.35 | 1.21 | 1.15 |
| ICC (latent variable method) | 0.030 | 0.029 | 0.012 | 0.007 |
| AIC | 111386 | 111292 | 110939 | 95598 |

[a] Adjusted for baseline deprivation, maternal age, education, race, prior preterm birth, and inter-birth interval. Interactions with age, inter-birth interval, and prior preterm birth set to mean covariate value.

PCV, proportional change in variance; MOR, median odds ratio; ICC, intraclass correlation

**Table 7. Evaluation of Positivity: Estimated Probabilities of Mobility Trajectories by Observed Trajectory**

| Estimated Probability of Mobility Trajectory, Mean (SD) | Observed Mobility Trajectory | | | | | |
|---|---|---|---|---|---|---|
| | High Upward | Intermediate Upward | No Change | Intermediate Downward | High Downward | Non-Mobile |
| High Upward | 0.35 (0.21) | 0.14 (0.14) | 0.07 (0.11) | 0.06 (0.10) | 0.07 (0.11) | 0.08 (0.13) |
| Intermediate Upward | 0.14 (0.08) | 0.18 (0.08) | 0.11 (0.09) | 0.09 (0.09) | 0.09 (0.08) | 0.08 (0.08) |
| No Change | 0.07 (0.05) | 0.12 (0.05) | 0.14 (0.06) | 0.12 (0.06) | 0.11 (0.06) | 0.10 (0.05) |
| Intermediate Downward | 0.06 (0.04) | 0.09 (0.05) | 0.12 (0.06) | 0.15 (0.07) | 0.15 (0.08) | 0.10 (0.06) |
| High Downward | 0.06 (0.07) | 0.09 (0.09) | 0.11 (0.10) | 0.14 (0.12) | 0.22 (0.16) | 0.09 (0.09) |
| Non-Mobile | 0.33 (0.16) | 0.38 (0.17) | 0.44 (0.19) | 0.44 (0.19) | 0.39 (0.18) | 0.55 (0.18) |

Trajectory probabilities were calculated by fixed effects logistic regression conditional on baseline tract, controlling for maternal age, education, race, baseline preterm birth, and inter-birth interval. The individual propensities were used to calculate the inverse probability of treatment for weights in the IPTW models.

**Table 8. Comparison of associations between mobility trajectories and baseline preterm birth to the associations with follow-up preterm birth**

| | Baseline Preterm Birth: Fixed Effects Model | | Follow-Up Preterm Birth: Fixed Effects Model | |
|---|---|---|---|---|
| | Crude | Fully Adjusted[a] | Crude | Fully Adjusted[b] |
| Mobility Trajectory | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) |
| High Upward | 0.91 (0.87, 0.96) | 1.01 (0.96, 1.06) | 0.84 (0.80, 0.88) | 0.93 (0.88, 0.98) |
| Intermediate Upward | 0.95 (0.91, 1.00) | 0.97 (0.92, 1.03) | 0.95 (0.91, 1.00) | 0.98 (0.93, 1.04) |
| No Change | 0.97 (0.92, 1.02) | 1.00 (0.95, 1.06) | 0.98 (0.93, 1.03) | 1.00 (0.94, 1.06) |
| Intermediate Downward | 1.03 (0.98, 1.08) | 1.03 (0.97, 1.08) | 1.09 (1.04, 1.15) | 1.04 (0.98, 1.09) |
| High Downward | 1.16 (1.11, 1.21) | 1.08 (1.03, 1.14) | 1.22 (1.17, 1.27) | 1.15 (1.09, 1.21) |
| Non-Mobile | ref | ref | ref | ref |

[a] Adjusted for maternal age, age2, education,and inter-birth interval length.

[b] Adjusted for maternal race, education, baseline preterm birth, age at baseline, and inter-birth interval length and set to mean values of interaction terms ( Age=26 years, No baseline preterm birth, 3 year inter-birth interval).

## Appendix A. Modeling Process

The modeling process proceeded, as described in the methods section, from collinearity assessment, to interaction, to confounding, and finally to precision assessment. This was done for the marginal and fixed effects model structures and collinearity, interaction, and confounding were assumed to be the same in the fixed and random effects conditional models. Baseline deprivation was not considered in the fixed effects model since tract-level factors cannot be considered using this structure.

The first marginal model that was attempted to be fit included all covariates (and interactions between each covariate and each mobility trajectory. Initial covariates included baseline deprivation, inter-birth interval, and first birth record measured maternal age, marital status, alcohol and tobacco use during pregnancy, highest education achieved, adequacy of prenatal care, Medicaid payment, parity, and preterm birth at 1$^{st}$ birth. This model was fit using SAS' PROC GENMOD with the baseline tract as the subject in the REPEATED statement and compound symmetric covariance structure. However, the number of parameters to be estimated in this model prohibited stable estimates from being made. An alternative strategy of fitting the model without interactions to identify covariates involved in collinearity problems was used. The initial model had three condition indices (CIs) over twenty, indicating three collinearity problems. The first, with the highest CI, involved the intercept, maternal age, and maternal age squared. This was avoided by centering age on its population mean, approximately 26 years. The second collinearity problem involved the intercept and maternal alcohol use during 1$^{st}$ pregnancy. Alcohol was dropped to avoid this problem.

The final problem involved maternal age, education, tobacco use during the first pregnancy, and parity. Parity was dropped, but the problem persisted. Tobacco use was then dropped, resolving all collinearity problems. The interaction terms were then added back into the model individually and separately to assess whether or not they created any further collinearity problems. No further collinearity problems were found. A limitation of this method is that it did not allow the assessment of collinearity between separate covariate-exposure interactions. After the collinearity assessment, the model contained the covariates baseline deprivation, maternal age and age-squared, marital status, education, prenatal care adequacy, prior preterm birth, Medicaid payment, inter-birth interval and race. Interactions between mobility trajectories and each covariate were retained as well.

Interaction terms were then assessed by testing the change in the QIC, which is the quasi-likelihood variant of the Akaike Information Criterion,[63] resulting from dropping each interaction individually and the Wald test p-value of each interaction. What constitutes a meaningful increase in QIC through a parameters inclusion is somewhat arbitrary, therefore the significance of the Wald test was given more weight for decision making. The full model had a QIC of 92,394. The least significant interaction was between maternal age-squared and exposure, marking it for exclusion from the model, but with retention of the age-exposure interaction. The second least significant interaction based on Wald test p-values was exposure-Medicaid. Dropping this interaction reduced the QIC by only 9. The next highest p-value was for the exposure-race interaction (p=0.82). Dropping this interaction as well as the exposure-Medicaid interaction lowered the QIC by 19. The next least significant interaction was between the

exposure and baseline deprivation quintile (p=0.66). Dropping this interactions, as well as the other two, lowered the QIC by 38, double the lowering by the other two interactions. The exposure-marital status interaction was the next least significant (p=0.47). Dropping this interaction, as well as the other three, resulted in a decrease of 44 in the QIC. The exposure-prenatal care adequacy interaction then had a p-value of 0.22 and was dropped, reducing the QIC by 54. The education-exposure interaction was the only remaining insignificant interaction (p=0.18) and was dropped, resulting in a final decrease in QIC of 64. Remaining significant interactions were between exposure and maternal age, prior preterm birth, and inter-birth interval.

The covariates not involved with interactions with mobility trajectories were then assessed as confounders through a backward elimination strategy with a 10% change in exposure-outcome association rule for retention, so that no covariates are included in the final model unless their exclusion results in a 10% change in an mobility trajectory odds ratio as measured in the full model. Dropping Medicaid payment, prenatal care adequacy, and marital status did not significantly change the exposure-outcome association estimates individually or as a chunk. Race, baseline deprivation, maternal age-squared, and education were then considered through dropping all possible subsets. Each subset dropped involved greater than 10% changes to at least one mobility trajectory-outcome odds ratio. Therefore, these three covariates were considered as confounders in the final model. The dropped covariates were re-included individually to assess their impact on exposure odds ratio precision through comparison of standard errors between model variations. No changes in precision were found. Therefore race, education, age-squared, and baseline deprivation only were included in the final model. Inter-birth interval,

baseline preterm birth, and baseline maternal age interactions with mobility trajectories were also included, as well as their respective lower-order terms.

The fixed effects model structure was then fit following a similar strategy using SAS's PROC SURVEYLOGISTIC with tracts identified in the CLUSTER statement and included in the model as dummy variables. A key difference was that this regression uses maximum likelihood based estimation, allowing likelihood ratio tests to be used to compare nested models. Collinearity was assumed to be the same between marginal and fixed effects models and was not re-assessed for the fixed effects model. Interaction was assessed in two chunks informed by the marginal model assessment. The first chunk tested the significance of interactions between exposures and baseline deprivation, Medicaid, marital status, and race. The likelihood ratio test resulted in a p-value of 0.98 indicating these interactions did not significantly increase the fit of the model and should be dropped. The next chunk tested included interactions of exposures and education, prenatal care adequacy, and prior preterm birth. The likelihood ratio test p-value for this test was 0.03, compared to the model dropping the first chunk. This indicates that some subset of this chunk is significant. The significance of the education and prenatal care adequacy interactions with exposure was tested and a p-value of 0.18 was found, indicating that these two can be dropped but the prior preterm birth interaction should be retained. The age and inter-birth interval interactions were tested individually and resulted in p-values of $<0.01$ each. The set of interaction terms were then the mobility trajectories and inter-birth interval, maternal age, and prior preterm birth, the same set as in the marginal model.

Confounding assessment followed the same strategy and 10% rule as in the marginal model strategy. It was found that all covariates aside from education and race could be dropped without significant changes in exposure odds ratios. Dropping education or race resulted in >10% changes in the most increased deprivation mobility trajectory only. The final model then included education and race as confounders and age, prior preterm birth, and inter-birth interval interactions with mobility trajectories. These are the same final model elements as in the marginal model, aside from baseline deprivation. The non-significance of baseline deprivation in the fixed effects model was to be expected since the variation in baseline deprivation within tracts (due to tract change over time) was much less than the variation in baseline deprivation between tracts. The within-tract variation is the only component of variation included in the fixed effects model. Based on this consideration, baseline deprivation was included in the final model for the random effects model structure even though it was not included in the fixed effects structure. Random effects models were fit with SAS's PROC GLIMMIX with the RANDOM statement used to indicate a random intercept for each tract and a compound symmetric covariance structure indicated. Precisions of exposure odds ratios were not changed by inclusion of any of the previously excluded covariates.