Comprehensive Mobility-Adjusted $PM_{2.5}$ Exposure and Health Outcome Assessment Across Pregnancy

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Project Summary

Ambient fine particulate matter ($PM_{2.5}$) exposure during the prenatal period has been consistently associated with adverse outcomes including preterm birth, low birth weight, and gestational hypertensive disorders. Notably, these associations are increasingly observed at concentrations below the U.S. Environmental Protect Agency (EPA) standards. Despite a growing body of literature, critical knowledge gaps remain. Prior studies often lack maternal health endpoints, maternal mobility in exposure assessment, and/or assessment of exposure at trimester-specific windows. The proposed study aims to evaluate how chronic and time-specific maternal exposure to ambient $PM_{2.5}$ affects both pregnancy and maternal health outcomes. To accomplish this, we will conduct a prospective cohort study enrolling 4,500 pregnant individuals from Brigham and Women's Hospital in Boston, MA, between 2027 and 2029. Ambient $PM_{2.5}$ concentrations will be estimated using high-resolution spatiotemporal models that incorporate EPA regulatory monitoring, satellite data, and land-use predictors. To improve exposure accuracy, residential and workplace addresses along with weekly mobility patterns will be collected at each trimester to generate mobility-adjusted exposure estimates. Outcomes of interest include preterm birth, low birth weight, stillbirth, loss of pregnancy, gestational diabetes, and preeclampsia. By integrating trimester-specific and mobility-adjusted exposure assessments with comprehensive maternal and fetal outcome data, this study will aim to advance $PM_{2.5}$ exposure methods and generate policy-relevant evidence of the effects of $PM_{2.5}$ exposure during critical preganancy windows. Our findings will aim to contribute to clinical guidance and environmental standards to better protect pregnant populations from ambient $PM_{2.5}$ exposure.

Public Health Relevance

Pregnant individuals in the United States (especially in high-traffic areas) and historically marginalized communities are routinely exposed to fine particulate matter ($PM_{2.5}$) at levels both above and below current federal standards. Exposure to $PM_{2.5}$ during pregnancy may increase the risk of adverse birth outcomes, including preterm birth, low birth weight, and pregnancy complications including preeclampsia and gestational diabetes. Therefore, understanding the effects of chronic, low-level exposure to $PM_{.25}$ during pregnancy is a critical public health issue and essential for improving maternal and child health outcomes.

Specific Aims

The body of literature examining the relationship between maternal exposure to fine particulate matter ($PM_{2.5}$) during pregnancy and adverse birth outcomes has been growing rapidly for the past 30 years. Much of the mechanistic literature points to oxidative stress and inflammation negatively impacting the growing fetus, as nutrients and oxygen are reduced in critical developmental windows during pregnancy. In terms of epidemiologic findings, adverse pregnancy outcomes have been associated with concentrations of $PM_{2.5}$ exposure at levels well below the current National Ambient Air Quality Standards (7 ug/m^3) from the U.S. Environmental Protection Agency (US EPA).

However, many of these studies are lacking either maternal health endpoints in addition to pregnancy outcomes or are lacking data on maternal mobility during pregnancy. **The objective of this proposed study is to assess the trimester-specific effects of maternal exposure to $PM_{2.5}$, including exposures at chronic low levels, on both pregnancy and maternal health outcomes.** The study cohort will be prospective, and will be enrolled at Boston's Brigham and Women's Hospital. The cohort will aim to enroll 4,500 participants over a 3 year period between 2027 and 2029 at the first prenatal visit. Data analysis will be conducted

between 2029 and 2031 for a total of five years. The study will aim to model ambient concentrations of $PM_{2.5}$ in conjunction with maternal addresses captured at a time point in each trimester to account for maternal mobility during pregnancy. Participants and their babies will be assessed for the following outcomes of interest: term birth weight, preterm birth, stillbirth, loss of pregnancy, gestational diabetes, preeclampsia, and eclampsia. The follow Specific Aims will be explored:

1. Examine the relationship between chronic exposure to $PM_{2.5}$ during pregnancy in Boston, MA and various pregnancy outcomes, including maternal health outcomes. Hypothesis: Mothers who experienced higher concentrations of $PM_{2.5}$ exposure across the length of their pregnancy will experience increased adverse pregnancy and maternal health outcomes.
2. Explore the relationship between specific adverse pregnancy outcomes and trimester-specific $PM_{2.5}$ concentration estimates to elucidate which trimesters are associated with certain adverse pregnancy outcomes. Hypothesis: All trimesters will be associated with at least one adverse pregnancy or maternal health outcome.

Significance

While Boston, Massachusetts has robust data collection efforts for air pollution and maintains traffic pollution that is under annual National Ambient Air Quality Standards (NAAQS), large disparities in exposure patterns exist for Asian, Hispanic, and Black populations in the city, both in terms of air pollution exposure *and* maternal birth outcomes.[1-4] In the past two decades, the body of literature on the linkages between ambient air pollution and adverse pregnancy outcomes has grown exponentially. The biological pathways for how and why fine

particulate matter (PM 2.5) affects the respiratory and cardiovascular systems have been studied since the late 1990s, but a gap in reproductive effects existed until more robust evidence for reproductive toxicity has only emerged in the last decade or so.

In a case-control study conducted in 2009 by Vera et. al, the association between exposure to particulate matter and its constituents (heavy metals and other substances) from vehicle traffic and adverse reproductive outcomes, including measures of fertility and significant reductions in birth weight.[5] In a large case-control study conducted by researchers in Los Angeles, California in 2007 demonstrated that exposure to $PM_{2.5}$ at high levels during the first trimester increased the odds of preterm birth in a range of 21-25%.[6] More trimester-specific evidence was gathered in a Connecticut- and Massachusetts-based study conducted by Bell at. al also in 2007. In both linear and logistic regression models, $PM_{2.5}$ was found to be associated with a 14.7 gram (-17.1 to -12.3, $p < 0.001$) decrease in birth weight per interquartile increase in pollution for the gestational period and 5.4% ($p < 0.05$) increased odds of low birthweight (under 2,500 grams), respectively.[7]

While these early studies demonstrated the linkage between $PM_{2.5}$ exposure and adverse birth outcomes, the toxicological mechanisms of these outcomes were misunderstood until the 2010s. In a study published in 2015 by Kim et. al, $PM_{2.5}$-induced oxidative stress and $PM_{2.5}$-accelerated production of reactive oxygen species was elucidated using human cell analysis in a laboratory setting.[8] Not only did the researchers find increased oxidative stress in the presence of $PM_{2.5}$, but microinjection of $PM_{2.5}$ into embryos caused severe mortality and impaired skeletal development.[8]

More recent toxicological and epidemiological evidence has refined our understanding of the reproductive effects induced by oxidative stress and the sensitive windows during gestation

for $PM_{2.5}$ exposure. A 2023 study conducted using participants enrolled in the Rhode Island Child Health Study (RICHS) found that increase in maternal $PM_{2.5}$ exposure (at an average level of 8μg/m^3) between 12 weeks before conception and 13 weeks' gestation had a significant inverse association with female infant birthweight percentiles (-7.40 [-14.78, -0.03]) suggesting that exposure in the early prenatal period may impact implantation and maternal blood flow mechanisms associated with birth weight.[9] Second and third trimester maternal exposures to PM2.5 are also thought to contribute significantly to low birthweight through mechanisms such as maternal pulmonary inflammation and placental inflammation, both of which can reduce oxygen and nutrition exchange to the fetus.[10] In addition, due to the variations in PM2.5 constituents, metals and polycyclic airol hydrocarbons (PAHs) can enter the maternal bloodstream and cause DNA damage to the fetus.[10]

Aside from the aforementioned New England-based epidemiologic studies on PM2.5 exposure and adverse pregnancy outcomes, Boston's urban setting, air pollution and maternal health statistics warrant improved maternal health education and policies. The latest *Health of Boston*: *Maternal and Infant Health Report* published in 2023 by the Boston Public Health Commission reported that the rate of LBW for Black infants (13.4%) was twice that of White infants (6.2%), and the percentage of PTB for Black mothers (13.8) was also double that of White mothers (7.1%).[4] Additionally, neighborhoods with higher percentages of Black residents, including Mattapan and Dorchester, had the highest percentages of LBW for 2019, 2020, and 2021 combined at 11.8% and 11.3%, respectively.[4] While these outcomes surely have multiple socioeconomic drivers, corresponding disparities in air quality over the last decade raise concerns about the possible effects $PM_{2.5}$ may be having on maternal health. A fact sheet released by the Union of Concerned Scientists in 2019 entitled "Inequitable Exposure to Air Pollution

from Vehicles in Massachusetts" modeled PM2.5 pollution by census tract combined with demographic information. Their findings indicated that major racial disparities in pollution patterns exist, as higher PM2.5 concentrations were higher for Asian (+36%), Black (+34%), and Hispanic (+26%) Americans than their white counterparts.[2]

The current EPA NAAQS for PM2.5 is 9 $\mu g/m^3$,[11] which is above the annual average PM2.5 concentration (7 $\mu g/m^3$) reported in the Massachusetts 2023 Air Quality Report.[1] However, the Air Quality Guidance (AQG) for annual PM2.5 concentrations from the World Health Organization is currently 5 $\mu g/m^3$, supporting the epidemiologic evidence that has found adverse health outcomes at chronic, low-level exposure to PM2.5.[12] Evidence using 2000 and 2010 census data suggests that non-Hispanic Black and urban Hispanic populations experience annual-average population-weighted PM2.5 concentrations of 8.4 $\mu g/m^3$ and 13.0 ppb (or 7.3 $\mu g/m^3$) in 2010, respectively.[13]

These disparities combined with relatively high levels of past exposure in Boston and the growing body of evidence of the relationship between PM2.5 exposure and adverse pregnancy outcomes suggests that more research is warranted in this field and in the Boston area. The aforementioned cohort studies lack mobility-adjusted exposure assessments and/or a combination of maternal and child health outcomes in the same study, which this proposal will aim to address.

Innovation

Our study will be the first study to our knowledge to incorporate maternal mobility in exposure assessment, maternal endpoints, and pregnancy outcomes in the same prospective cohort. Many of the previous studies examining the relationship between prenatal $PM_{2.5}$ exposure and adverse pregnancy outcomes have only included outcome measures of the fetus itself,

including measures of birth weight, gestational age, stillbirth, and loss of pregnancy. Often, studies that examine maternal health outcomes like gestational diabetes and preeclampsia are conducted separately, which innately remove the ability to determine relationships between prenatal $PM_{2.5}$ exposure, maternal outcomes, and birth outcomes, all of which are imperative to understanding the underlying mechanisms of $PM_{2.5}$ exposure and adverse reproductive outcomes.

Additionally, this proposed study addresses a common gap in the exposure modeling techniques, which is that most do not include maternal mobility over the course of the pregnancy. Our exposure assessment will benefit greatly from the increased precision that will result from the mobility-adjusted exposure measurements we are able to produce by capturing residential address and mobility patterns at each trimester. Ostensibly, maternal mobility exposure assessment has not been combined with both maternal and birth outcomes in the same study due to the volume of endpoints that will be produced along with the work to integrate mobility with $PM_{2.5}$ modeling data.

Much of the current literature on $PM_{2.5}$ exposure during pregnancy focuses on regions where exposure is either very high, very acute in duration, or both. While the city of Boston has relatively low annual average $PM_{2.5}$ concentrations that are below EPA regulatory standards, studying exposures at a chronic, low-level addresses a critical gap in $PM_{2.5}$ exposure science in two ways. First, international guidelines and research has consistently suggested current EPA NAAQS are too high, with the World Health Organization setting annual average limits 4 ug/m^3 lower than the EPA. Second, chronic low-level exposures are more common in and representative of rural and suburban $PM_{2.5}$ average exposure concentrations, suggesting that while a study conducted in an urban area like Boston may not be wholly generalizable to rural

regions, it addresses a knowledge gap in maternal health and pregnancy outcomes at levels lower than the national regulatory standards.

Finally, more prospective cohort studies are needed in the area of air pollution exposure and reproductive health outcomes. While there is robust historical air monitoring data and existing maternal and child health cohorts, it is critical to create new cohorts that utilize more precise exposure assessment data, reduce bias, and capture adequate socioeconomic status, racial, ethnic, and gender data. Due to the high volume of outcome measures that will be captured by this study, it is critical to have control over all covariates and effect measure modifiers from the outset, which will be most achievable when using a prospective cohort design.

Approach

Overview

This study will aim to enroll approximately 4,500 participants and create a new prospective cohort with data on outcomes including preeclampsia, gestational diabetes, birth weight, preterm birth, gestational age, stillbirth, and loss of pregnancy. Exposure estimates will be based on data from EPA fixed-site monitors and NASA satellite data that will be integrated using a land use regression model. A structured questionnaire on maternal mobility patterns during pregnancy will be used to assess and integrate mobility patterns into the exposure assessment, resulting in mobility-adjusted $PM_{2.5}$ estimates in each trimester for each participant. We will evaluate the trimester-specific association between mobility-adjusted $PM_{2.5}$ exposure and adverse maternal and fetal outcomes using multivariable regression analyses, stratified analyses, and sensitivity analyses, adjusting for potential confounding from key covariates.

Study Population

This study will aim to enroll pregnant individuals aged 18 to 40 during their first prenatal visit at the Brigham and Women's Hospital in Boston. Participants will be limited to ages 18 to 40, which lies within the range of "reproductive age" according to the World Health Organization, but excludes participants older than 40 to limit any potential effect modification on adverse pregnancy outcomes by age.[14] Participants will be required to be Boston residents as the catchment area of the study - and where ambient $PM_{2.5}$ concentrations will be captured - will be the city of Boston.

Based on the *Obstetrical Care Disclosure Statement* for fiscal year 2020 released by the Brigham and Women's Department of Obstetrics and Gynecology, the hospital sees approximately 6,200 deliveries each year. Based on this number, this study will aim to enroll and follow approximately 1,500 participants per year for a total cohort of 4,500 participants over an almost three year period (January 2027 - August 2029).

Exposure Assessment

Participants will be assessed during their initial prenatal visits according to the Brigham and Women's "typical visit" metrics, which include weight measurement, blood pressure, uterine measurement (fetal growth), physical exam, urine sample for sugar and protein levels, fetal heart rate, and blood tests when necessary. All data for this study will be collected at the initial visit, a 12-week visit (first trimester), a 24-week visit (second trimester), a 30-week visit (third trimester), and at the date of delivery or the end of the pregnancy if not a live birth.[15] Along with the physical exam measures, participants will be asked a structured mobility questionnaire at each visit, which will encompass domains including home and residential details, daily mobility and activity spaces, and special events or changes in mobility patterns. Time spent at each

location will be measured using hours per day and will include locations such as work, school, transportation, and “other”.

Mobility questionnaire data will be collected to adjust the primary exposure measures of ambient $PM_{2.5}$ concentrations. To ensure these primary data is as precise as possible, a combination of EPA monitoring data and satellite-derived aerosol optical depth (AOD) from NASA’s Moderate Resolution Imaging Spectroradiometer (MODIS) instruments will be integrated utilizing spatiotemporal modeling:

1. *EPA Monitoring Data:* EPA’s Air Quality System (AQS) fixed-site monitors will provide daily $PM_{2.5}$ concentration data, which are high-quality and ground-level measures of $PM_{2.5}$. This data will be incredibly useful for ensuring highly precise Boston-specific monitoring is incorporated into the exposure assessment. However, according to the current EPA AirData Air Quality Monitors map, there are only five active EPA monitors for $PM_{2.5}$ currently.[16]

2. *NASA MODIS Data:* To supplement the gaps in the EPA AQS data, we will incorporate satellite-based AOD data from NASA’s MODIS instruments. MODIS monitors ambient aerosol concentrations and calculates its thickness by measuring columnar atmospheric pollution.[17] However, MODIS data collected by satellite can be influenced by weather patterns including cloud cover and surface reflection, reducing its precision in exposure modeling on its own. Therefore, MODIS data will be used to supplement the ground-level EPA monitoring data.

3. *Spatiotemporal Modeling and Data Integration:* To integrate these data sources, we will employ a land use regression (LUR) modeling framework to predict daily $PM_{2.5}$ concentrations at a 1 kilometer by 1 kilometer spatial resolution across the Boston city limits. This model will utilize predictor variables like elevation, seasonal indicators, land use categories (residential,

commercial, etc.), traffic density, and others, as well as machine learning techniques like random forest to ultimately produce integrated, gridded exposure data.

Exposure estimates will be assigned to each participant based on residential addresses collected at the first prenatal visit and at each trimester visit, as well as workplace addresses and time-location data obtained through the mobility questionnaires. Daily $PM_{2.5}$ predictions will be averaged over trimester windows (1st trimester: conception to 13 weeks (conception calculated as 14 days after the last menstrual period); 2nd trimester: 14 weeks to 27 weeks; 3rd trimester: 28 weeks to delivery) and weighted by the proportion of time spent at each location to create a mobility-adjusted exposure metric.

Outcome Assessment

The outcomes assessed in this study will include two measures of maternal health (gestational diabetes) and four measures of fetal/pregnancy health (birth weight, preterm birth, stillbirth, and loss of pregnancy). All outcomes will be captured as a part of the prenatal visits and/or at the time of delivery or end of pregnancy. Because hospital data will be utilized for all outcome measures, even if diagnoses like gestational diabetes or preeclampsia occur at visits that are not one of the specified trimester visits for the study, the study team will have access to the dates of these diagnoses and will be able to assign the appropriate trimester to each outcome.

Binary outcome measures will include gestational diabetes (yes/no), preeclampsia (yes/no), stillbirth (yes/no), and loss of pregnancy (yes/no). Birth weight data will be collected as a continuous variable and will also be used to assess low birth weight (yes/no), using the 2,500 gram metric. Additionally, preterm birth will be assessed as a binary variable (yes/no) but will also be accompanied by gestational age, which will be a categorical variable (weeks).

Covariates and Mediators

We will be collecting data on covariates using both the intake information gathered by Brigham and Women's Obstetrics staff during routine prenatal visits (maternal age, race/ethnicity, pre-pregnancy BMI, smoking status, parity, season and year of conception) as well as additional information gathered using questionnaires by trained study staff (maternal income, housing type, education). We will adjust for a set of these a priori confounders, which were selected based on existing literature. These variables may influence both $PM_{2.5}$ exposure and pregnancy outcomes and will be included in all multivariable models to reduce confounding.

We will also assess potential effect modification of the association between trimester-specific, mobility-adjusted $PM_{2.5}$ exposure and maternal and fetal outcomes by key demographic and exposure-related factors. Specifically, we will test for interaction by maternal age, race/ethnicity, pre-pregnancy BMI, smoking status, alcohol use, parity, socioeconomic status, and co-exposure with other air pollutants (O_3, PM_{10}, and NO_x, all of which can be modeled using EPA monitors and NASA MODIS modeling). These variables were selected based on biological plausibility and the aforementioned evidence of disparities in exposure in Boston by race and socioeconomic status. Interaction terms will be included in regression models and stratified analyses will be conducted for modifiers with statistically significant ($p < 0.05$) to characterize the effect. Sensitivity analyses will be discussed in further detail in the Statistical Analyses section.

Statistical Analyses

All statistical analyses will be performed using SAS (v.9.4 or later). Descriptive statistics will be generated to assess the distribution of all variables prior to model fitting, and statistical significance will be defined as $p < 0.05$.

Exploratory data characterizations: We will begin the statistical analysis phase of the study by assessing the distributions of both outcome and exposure variables using histograms, kernel density plots, and Q-Q plots. We will test for normality using the Shapiro-Wilk test and assess variance homogeneity using Levene's test where appropriate. In terms of exposure variables, we will assess linearity in the exposure-response relationship for continuous $PM_{2.5}$ concentrations using restricted cubic splines and use smoothing techniques to inform later model structuring. In the case that non-normality is detected in continuous outcomes (i.e. birth weight), we will explore log transformations or generalized linear modeling. For binary and categorical outcomes, logistic regression will be used regardless of distribution.

Primary analyses: We will assess the relationship between maternal exposure to $PM_{2.5}$ during pregnancy and adverse pregnancy and maternal health outcomes using regression modeling. Logistic regression will be used for binary outcomes, which include preterm birth, gestational diabetes, preeclampsia, stillbirth, and loss of pregnancy. Linear regression or generalized linear models will be utilized to assess the relationship between $PM_{2.5}$ exposure and birth weight (continuous), depending on the results of the distribution assessment.

$PM_{2.5}$ exposure will be modeled as both a continuous variable (in ug/m^3) to assess the dose-response relationship, and as a categorical variable (quantiles) to assess potential thresholds for adverse outcomes. In the instance that the initial regression models using a continuous exposure results in a non-linear association, we will utilize quantiles to categorize $PM_{2.5}$ exposure.

All models will be considered multivariable regressions, as each will be adjusted for key covariates that may confound the relationship between $PM_{2.5}$ exposure and adverse outcomes. These will include maternal age (18 - 25, 26-34, >/ 35), race/ethnicity (White, Black, Hispanic,

Asian, Other), socioeconomic status (education), pre-pregnancy BMI (underweight, normal weight, overweight, obese), smoking status (yes/no), alcohol use (yes/no), parity (nulliparous/multiparous), and season (Spring, Summer, Autumn, Winter) of conception.

Effect modification and interaction tests: To evaluate whether the association between maternal $PM_{2.5}$ exposure and adverse pregnancy and maternal health outcomes varies across population subgroups, we will test for effect modification using both multiplicative and stratified approaches. We will include interaction terms in the regression models between $PM_{2.5}$ exposure (both continuous and categorical) and potential effect modifiers. Effect modifiers will include maternal age, race/ethnicity, pre-pregnancy BMI, smoking status, socioeconomic status, and other co-pollutants (O_3, PM_{10}, NO_x, modeled as continuous and categorical). Interaction terms will be assessed in the adjusted multivariable models using likelihood ratio tests or Wald tests to determine whether inclusion of the interaction term significantly improves the model fit (utilizing a $p < 0.05$ significance level).

Where statistically significant interaction is observed, we will conduct stratified analyses by level of the effect modifier to estimate stratum-specific associations and assess patterns of vulnerability. All interaction analyses will be performed separately for each outcome and trimester-specific exposure window.

Sensitivity analyses: Additional sensitivity analyses will be performed to explore the robustness and validity of our primary findings.

Mobility: We will compare effect estimates derived from mobility-adjusted $PM_{2.5}$ exposures (weighted by time spent at home, work and other locations) to those based solely on residential address.

Health Status: We will re-run primary models excluding participants with chronic pre-existing health conditions (i.e. diabetes, hypertension, cardiovascular disease) to evaluate whether baseline health status confounds observed associations between $PM_{2.5}$ exposure and pregnancy outcomes. Results will be compared to full-cohort estimates.

Exposure Window: To assess the impact of exposure window definitions, we will estimate $PM_{2.5}$ exposure using alternative windows such as 4-week averages and monthly intervals in addition to trimester-specific and whole pregnancy average exposures.

Limitations and Strengths

This study design is not without limitations. While this study design presents a very complex and refined exposure assessment method, there is still the potential for exposure misclassification, This is largely due to the fact that despite refinements, $PM_{2.5}$ exposure will still be modeled, and as such will not be a direct assessment of personal exposure that might be captured using personal monitoring techniques. There is also the possibility of residual confounding, especially with more ambiguous measures like socioeconomic status that might be fully capturing all possible measures of income, race, housing, etc. Residual confounding will be addressed in part with covariate adjustments where appropriate, but will likely not be completely accounted for.

The largest limitation of this study is selection bias due to the fact that pregnant people receiving prenatal care at the Brigham and Women's Hospital in Boston may systematically differ in terms of socioeconomic status and race than those who do not receive this care. This limitation is addressed in-part by the relatively large cohort size, but cannot be dismissed. Finally, the findings from this cohort may not be generalizable to rural regions of the United

States or regions with high $PM_{2.5}$ concentrations, as Boston is an urban city with robust healthcare and low average annual $PM_{2.5}$ concentrations.

This study design does have a number of strengths. The large sample size will ostensibly give more statistical power to the findings of this study. Additionally, the trimester-specific outcome data may give insight into critical windows of vulnerability to $PM_{2.5}$ exposure during pregnancy, which may improve mechanistic understandings of this exposure pathway and lead to trimester-specific guidelines and policies. Also, the inclusion of maternal mobility in the exposure assessment improves its accuracy and is innovative for a study of this size. Furthermore, this comprehensive study design that includes both maternal and child health outcomes increases the robustness of this cohort's data for future analyses, including those that identify mechanisms of adverse pregnancy outcomes and air pollution exposure.

This study also examines chronic and relatively low-level $PM_{2.5}$ exposure, which fills a critical evidence gap in the current literature. By demonstrating adverse pregnancy outcomes at concentrations below current EPA NAAQS, these findings could produce highly policy-relevant findings that will be impactful for both regulatory science and risk communication. The prospective cohort design and inclusion of socioeconomic and race covariate data will enable future researchers to conduct research analyzing the specific effects of race and socioeconomic status on mobility-adjusted $PM_{2.5}$ exposure during pregnancy, which may contribute to furthering our understanding of the role played by race in the relationship between chronic low-level prenatal $PM_{2.5}$ exposure and adverse pregnancy outcomes.

<u>Study Timeline</u>

January 2027: Begin enrolling participants at the Brigham and Women's Hospital

August 2029: End enrollment and close out data collection efforts

September 2029: Begin exposure assessment and initial data cleaning and statistical analyses

2030: Initial manuscript on preliminary findings

2031: Additional manuscript(s) and advanced statistical analyses based on preliminary findings

Human Subjects

This study aims to enroll approximately 4,500 women aged 18 to 40 years old. Participants will be given detailed informed consent by study staff who have gotten the necessary Institutional Review Board (IRB) approval from both the Brigham and Women's Hospital and Boston University IRBs. There are minimal risks associated with participation in this study as the data that will be collected is not beyond the scope of information that will already be obtained during normal prenatal visits at the Brigham and Women's Obstetrics care protocols.

There is potential for a breach of patient confidentiality associated with this study, but participants will be given a unique study ID in the form of 4 numbers to remove any identifiable information from their study files. Additionally, files will be stored using encrypted, password protected data storage platforms and paper forms will be kept in locked filing cabinets only accessible to study staff.

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