EPA Public Access

Author manuscript

Environ Res. Author manuscript; available in PMC 2020 March 01.

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Published in final edited form as:

Environ Res. 2019 March ; 170: 178–186. doi:10.1016/j.envres.2018.12.013.

Preterm Birth and Economic Benefits of Reduced Maternal Exposure to Fine Particulate Matter

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Abstract

Preterm birth (PTB) is a predictor of infant mortality and later-life morbidity. Despite recent declines, PTB rates remain high in the United States. Growing research suggests a possible relationship between a mother's exposure to common air pollutants, including fine particulate matter (PM_{2.5}), and PTB of her baby. Many policy actions to reduce exposure to common air pollutants require benefit-cost analysis (BCA), and it's possible that PTB will need to be included in BCA in the future. However, an estimate of the willingness to pay (WTP) to avoid PTB risk is not available, and a comprehensive alternative valuation of the health benefits of reducing pollutant-related PTB currently does not exist. This paper demonstrates an approach to assess potential economic benefits of reducing PTB resulting from environmental exposures when an estimate of WTP to avoid PTB risk is unavailable. We utilized a recent meta-analysis, county-level air quality data and county-level PTB prevalence data to estimate the potential health and economic benefits of a reduction in air pollution-related PTB, with PM_{2.5} as our case study pollutant. Using this method, a simulated nationwide 10% decrease from 2008 PM_{2.5} levels resulted in an estimated reduction of 5,016 PTBs and benefits of at least \$339 million, potentially reaching over one billion dollars when considering later-life effects of PTB.

Keywords

air pollution; preterm birth; benefits; PM_{2.5}

1. Introduction

Preterm birth (PTB), or birth before 37 weeks of gestation, is a leading predictor of infant mortality (MacDorman et al., 2013) and an important contributor to later-life disease and disability (Institute of Medicine, 2007; National Guideline Alliance, 2017; Petrou, 2018; Platt, 2014; Raju et al., 2017). Prior analysis suggests that the high rate of infant mortality

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Declarations of interest: none

(OECD, 2018) in the United States (U.S.), which ranks among the highest of countries belonging to the Organization for Economic Cooperation and Development, may largely be due to a high PTB rate, and decreasing the PTB rate could thereby significantly reduce infant mortality in the U.S. (MacDorman and Mathews, 2009). Research is also increasingly linking PTB to a broad array of childhood and later-life health outcomes, including neurodevelopmental, respiratory, digestive, immunological, and cardiovascular problems (Institute of Medicine, 2007; National Guideline Alliance, 2017; Petrou, 2018; Platt, 2014; Raju et al., 2017).

A growing body of evidence suggests a relationship between a mother's exposure to environmental contaminants during pregnancy and PTB of her baby (Stieb et al., 2012; Stillerman et al., 2008; Sun et al., 2015). The most extensive evidence of this relationship is for ambient air pollution. Six pollutants—carbon monoxide, lead, nitrogen dioxide, ozone, particulate matter (PM), and sulfur dioxide—commonly found across the U.S. are designated as “criteria air pollutants” under the Clean Air Act. The U.S. Environmental Protection Agency (EPA) currently considers existing evidence to be suggestive of a causal relationship between exposure to five of the six criteria pollutants and reproductive, developmental, and/or birth outcomes (U.S. Environmental Protection Agency, 2009; U.S. Environmental Protection Agency, 2010b; U.S. Environmental Protection Agency, 2013b; U.S. Environmental Protection Agency, 2013c; U.S. Environmental Protection Agency, 2016b), with sulfur dioxide as the exception (U.S. Environmental Protection Agency, 2017b). The potential relationship between these criteria pollutants and PTB is especially concerning because a) by nature of the common presence of criteria pollutants, exposure is often unavoidable; and b) a disproportionate burden of exposure may be placed on individuals in disadvantaged communities, who are already subjected to multiple socioeconomic and health inequities (Bell and Ebisu, 2012; Clark et al., 2017; Federal Interagency Forum on Child and Family Statistics, 2016; Hajat et al., 2015; Mikati et al., 2018; Miranda et al., 2011).

Regulations promulgated under the Clean Air Act to limit or reduce exposure to criteria pollutants are subject to many requirements by statute, executive order, and EPA policy. Though benefit-cost analysis (BCA) for setting health-based primary National Ambient Air Quality Standards (NAAQS) is not required by the Clean Air Act, it has been required for economically significant regulations—those with an annual effect on the economy of \$100 million or more—by a series of executive orders dating back to 1981 (Carey, 2014). As such, BCA has typically been conducted for primary NAAQS determinations and for other economically significant rulemakings involving criteria pollutants or their precursors.

Estimating human health benefits of reducing any exposure requires health risks to be quantified and then valued in monetary terms, but data limitations, as well as analytic choices in risk assessment, often preclude full quantification and valuation (McGartland et al., 2017). The lack of quantification for many health outcomes, including adverse birth outcomes such as PTB, poses a challenge for conducting complete BCAs of reducing harmful environmental exposures. Additionally, the preferred valuation measure for BCA is willingness to pay (WTP) for risk reduction, defined as the maximum amount of income one would give up to obtain a reduction in risk to one's health (U.S. Environmental Protection

Agency, 2010a). In principle, WTP for reduced risk reflects all consequences of the full set of health effects associated with a given reduction in exposure, but many health effects, including PTB, lack an estimate of WTP in the economics literature (U.S. Environmental Protection Agency, 2010a). An alternative, less comprehensive valuation approach is to focus on the costs avoided from expected reduced incidence in the population. This requires an estimate of the direct and indirect costs associated with PTB, such as incremental costs from birth hospitalization and medical care in infancy, special education, lost wages or productivity, and later-life health complications (Jo, 2014). However, few studies exist on the economic costs of PTB, and these generally focus on costs during the neonatal period or the first few years of life, omitting any costs later in life (Grosse et al., 2017; Institute of Medicine, 2007; Jacob et al., 2017; Petrou, 2018). These issues hinder identifying and adopting the most efficient or cost-effective policies and have been recognized by the Institute of Medicine (IOM), which, in its 2007 report on PTB, recommended investigation into the economic consequences of PTB in order to better evaluate policies for its prevention and treatment.

To date, EPA has not included PTB in any BCA. EPA practice for benefits analysis of criteria pollutant regulations is to consider for inclusion those effects with evidence judged to be “causal” or “likely causal.” EPA’s most recent Integrated Science Assessment (ISA) of PM, published in 2009, did not report a summary evidence conclusion for PTB specifically, but it did conclude that the evidence for reproductive and developmental outcomes overall, including PTB, low birth weight, birth defects, and infant mortality, was considered to be “suggestive of a causal relationship,” indicating a lower level of confidence than a “causal” or “likely causal” conclusion (U.S. Environmental Protection Agency, 2009). Further research on PM_{2.5} and PTB has been published since completion of the 2009 ISA (Ha et al., 2014; Kloog et al., 2012; Lavigne et al., 2018; Pereira et al., 2014; Wu et al., 2016), and an updated ISA incorporating newer evidence is projected to be completed in 2019 (U.S. Environmental Protection Agency, 2016a). With the developing evidence for environmental contaminants—especially air pollution—and PTB, it may be warranted to include PTB in a BCA in coming years. How this would be done, however, is not immediately apparent, because of the aforementioned data limitations and complications regarding the many potential health outcomes also related to PTB.

This study outlines a framework and methodology to examine the potential economic benefits arising from reducing PTBs resulting from environmental exposures. To illustrate the process, environmental exposures of interest were first narrowed down to criteria pollutants because a) there are high potential benefits of reducing PTB associated with criteria pollutant exposure, due to their widespread human exposure; b) with rapid growth of the literature in recent years, there are now many studies of criteria pollutants and PTB, including meta-analyses; and c) well-established tools and methods for benefits analysis of these pollutants are available. We present a case study of maternal exposure to PM_{2.5} to demonstrate a proposed approach to estimating the potential health and economic benefits of reducing pollutant-related PTB.

2. Methods

Our approach to quantifying a PM_{2.5}-related reduction in PTB and the associated economic benefits involves first calculating the reduction in number of PTB cases attributable to decreased ambient PM_{2.5} levels, followed by valuation (monetization) of immediate and later-life consequences of the reduced PTB cases.

2.1. Calculation of Reduced Cases and Immediate Benefits in BenMAP

The Environmental Benefits Mapping and Analysis Program – Community Edition (BenMAP-CE or BenMAP) is an EPA computer program that quantifies and monetizes the health impacts of air pollution. BenMAP integrates exposure, population, and health data across a given space and enables translation of a health effect estimate into risk per increment of exposure (Sacks et al., 2018). This study utilized BenMAP to estimate the potential PTB benefits of a reduction of ambient concentrations of county-level PM_{2.5} nationwide. Because BenMAP does not include data for Alaska or Hawaii, this analysis is conducted for the contiguous U.S., and any mention of U.S. or national data or analyses in this paper hereafter refers to the contiguous U.S.

The impact of the air quality change on PTB was calculated within BenMAP by specifying the input factors seen in equation (1), the logistic health impact function used for this study, where y is the annual reduction in PTBs; y_0 is the annual baseline prevalence rate of PTB; β is the coefficient relating PM_{2.5} and PTB; $\Delta PM_{2.5}$ is the simulated change in PM_{2.5} concentration; *population* is the number of women ages 15 to 44; and *fertility rate* is the number of live births per year per woman ages 15 to 44.

$$y = y_0 \cdot \left[1 - \frac{1}{(1 - y_0) \cdot e^{\beta \cdot \Delta PM_{2.5}} + y_0} \right] \cdot \text{population} \cdot \text{fertility rate} \quad (1)$$

Health impact and valuation results were first calculated at the county level and then aggregated to provide state-level and national estimates. We assume, as do many applied analyses, that the relationship between PM_{2.5} and preterm birth is linear within the range of real-world exposures. However, different concentration-response functional forms would affect both the total benefits and the distribution of those benefits. For example, a sublinear function would result in more benefits estimated in areas of relatively high PM_{2.5} concentrations, while a supralinear function implies higher benefits in cleaner areas (Pope et al., 2015).

2.1.1. Exposure—Daily 24-hour mean PM_{2.5} measurements reported to the EPA Air Quality System from ambient air monitoring stations were used to estimate baseline county-level air quality. BenMAP uses the Voronoi Neighborhood Averaging (VNA) method to interpolate multiple stationary monitor point values to a county-wide air quality estimate (U.S. Environmental Protection Agency, 2017a). The VNA method calculates an inverse-distance weighted average of the closest monitors surrounding a county's center to represent

the county's overall $PM_{2.5}$ level, regardless of whether these monitors are inside the county or not. (Predicted estimates tend to be less reliable in rural or remote areas due to fewer monitors being present (Fann and Risley, 2013; Hubbell et al., 2005). These data inherently represent smaller populations with few to no alternative measurements available, and measurement error was expected to be negligible for the purposes of this study). $PM_{2.5}$ measurements were taken from approximately 1,000 monitors in 2008, the most recent year for which EPA provided BenMAP-compatible air quality data at the time of this study. For this analysis, we simulated a 10% decrease in 2008 annual average county-level $PM_{2.5}$ concentrations across the country (U.S. Environmental Protection Agency, 2017c).

2.1.2. Population and fertility rate—The population of interest was women in the U.S. ages 15 to 44. Population data were programmed within BenMAP and originally derived from and predicted based on U.S. Census data (U.S. Environmental Protection Agency, 2017a). The Centers for Disease Control and Prevention (CDC) defines fertility rate as the number of births per woman ages 15 to 44 in a given year (Centers for Disease Control and Prevention, 2016). Multiplying the population of women ages 15 to 44 by fertility rate yielded a unit of all births, or the denominator of the prevalence rate. All data were 1) at the county level and 2) from 2008 to match the most recent BenMAP-compatible air quality data.

2.1.3. Baseline prevalence rates—The numbers of PTBs and all births in each county were obtained from CDC WONDER for 2008. County-level baseline prevalence rates (y_0) were calculated as all PTBs divided by all births in each county. The PTB and all birth values for any counties with a population of less than 100,000 in a given state were grouped together in CDC WONDER as “Unidentified Counties” of the state. Any data representing a county with fewer than 10 births were suppressed in CDC WONDER. To represent rates for unidentified counties or counties with suppressed data, the statewide rates from the grouped Unidentified Counties were used.

2.1.4. Health impacts—The β coefficient of the health impact function relating $PM_{2.5}$ and PTB was derived from a 2015 meta-analysis by Sun et al. (2015) of studies measuring the association between $PM_{2.5}$ and PTB. Sun et al. included 18 studies conducted mostly in North America, Europe, and Australia, overall totaling over three million study participants. Effect estimates from each study were extracted and converted to regression coefficients per $10 \mu g/m^3$ increase in $PM_{2.5}$ to obtain a pooled estimate. The authors reported results for PTB as pooled odds ratios (ORs) per $10 \mu g/m^3$ increase in $PM_{2.5}$ for varying exposure periods, exposure assessment methods, and study types. Thirteen of the aforementioned 18 studies included exposure data for the entire pregnancy. The pooled OR for maternal exposure to $PM_{2.5}$ during the entire pregnancy, derived from these 13 studies, was 1.13 (95% confidence interval (CI): 1.03, 1.24). We converted the central estimate of this pooled OR to a logistic regression β coefficient of 0.012 relating risk per $1 \mu g/m^3$ increase in $PM_{2.5}$ by using the general formula $\ln(OR) = \beta \cdot \Delta PM_{2.5}$ as illustrated in the BenMAP User Manual Appendices (U.S. Environmental Protection Agency, 2017a).

As a sensitivity analysis, we converted the lower and upper bounds of the CI to β coefficients ($\beta = 0.003, 0.022$) to calculate reduced cases using these alternative coefficients.

2.1.5. Economic valuation—The monetized benefits of the reduction in PTB resulting from the simulated air quality improvement were calculated within BenMAP, which applies a given valuation function to the cases of PTB calculated by the health impact function. Ideally, the analysis would employ a WTP value for reduced risk of PTB that would account not just for medical costs and lost productivity, but for all or most of the expected consequences associated with PTB, including long-term health consequences and any intangible effects on quality of life. However, we are aware of no such estimates in the economics literature. A second-best valuation strategy, which we adopt here, is to first estimate the immediate or early-life cost of illness (COI) associated with PTB and then to add the present value of costs associated with longer-term consequences.

For our primary analysis, we draw upon the IOM's report on PTB which included a COI estimate representing an average over all PTBs in 2005 dollars with costs after the first year of life discounted at a 3 percent rate. The report estimated costs for several consequences of PTB; for each of these consequences, the estimate represents the average cost of each PTB incremental to the average cost of a term birth. The COI included all incremental medical care costs from birth to age 5 years; incremental maternal delivery costs; early intervention costs, or costs of targeted services for children from birth to age 3 who have developmental delays or other delay-related health conditions; and medical care, special education, and individual lost productivity costs for the following four developmental disabilities (DDs), experienced by a subset of individuals born preterm and averaged over all PTBs, for ages 6 and older: cerebral palsy, intellectual disability (mental retardation), vision impairment, and hearing loss. These values are described in Table 1. The cost estimate for each category was converted to 2014 dollars within BenMAP.

It is important to note that this PTB COI estimate does not account for several significant cost categories, such as costs after age 5 outside of those for the four aforementioned DDs or lost productivity costs for the parents of the person born preterm, thereby underestimating the value of reduced PTB (Institute of Medicine, 2007). For a more complete estimate of the value of reducing PTB, some additional PTB-related costs were estimated, as detailed in the next section. Furthermore, although the estimates from the IOM report have been widely used in the literature, the report also includes recommendations for refined analyses that would improve the accuracy of their estimates. These recommended improvements include undertaking multivariate modeling to better understand the large variance in economic burden across the population and performing analyses of the effects of race, ethnicity, and/or socioeconomic status on this burden.

2.2. Supplemental Analysis: Additional Benefits of Reduced PTB

Additional later-life outcomes of PTB were assessed for availability of adequate data on 1) evidence of their association with PTB, and 2) the WTP to reduce or avoid the later-life outcome or the COI of the outcome. Little or no information was found quantifying WTP or COI in the U.S. for most post-neonatal health outcomes, effects on familial dynamics, or

earnings and education outside those already quantified by the IOM. However, the available data for intelligence quotient (IQ) deficits, asthma, and diabetes mellitus (types 1 and 2) included WTP or COI data as well as meta-analyses of their relationship with PTB, and thus were deemed adequate for the analysis. Benefits calculations were performed at the national level to provide a broad overview of these potential benefits. All values are present values discounted at 3 percent and are expressed in 2014 dollars.

2.2.1. Cognitive benefits: IQ—Kerr-Wilson et al. (2012) conducted a meta-analysis of the relationship between PTB defined as both a binary variable (preterm vs. term) and a categorical variable (extremely, very, and moderately preterm, or <28, 28–31, and ≥32 weeks vs. term) and IQ deficits. The meta-analysis included 27 studies of 7,044 children total. The average gestational age of the preterm subjects in many of the studies was lower than that of PTBs in the U.S. overall. Because babies born preterm are on average moderately preterm—i.e. fewer babies are born at increasingly lower gestational ages—the moderately preterm category was used rather than the binary preterm category. Moderately preterm babies had a weighted mean IQ score 8.4 (95% CI: 6.6, 10.2) points lower than that of term babies.

EPA has routinely valued the benefits of avoided IQ decrements based on the effect of IQ on lifetime earnings, as was done to estimate the cognitive benefits of reduced exposure to lead and methylmercury. In the most recent application (U.S. Environmental Protection Agency, 2015) of this model, EPA derived average lifetime earnings values from U.S. Census data and used estimates from Salkever (1995) to calculate an economic cost of \$15,884 for each IQ point loss. EPA has also used Schwartz (1994) estimates to derive \$11,559 per IQ point; however, Salkever (1995) was re-examined in 2014 (Salkever, 2014) and deemed to be better suited for use in the present analysis.

As a sensitivity analysis, we carried through the calculations using the lower and upper bounds of the CI of weighted mean IQ decrement for moderately preterm babies.

2.2.2. Asthma—Sonnenschein-van der Voort et al. (2014) evaluated the relationship between PTB and school-age asthma defined as “asthma diagnosis reported between 5 and 10 years (no, yes),” preferably physician diagnosed, across 18 studies of European cohorts. The meta-analysis reported a pooled OR of 1.40 (95% CI: 1.18, 1.67). This OR and the prevalence of PTB and asthma (U.S. Environmental Protection Agency, 2013a) were used to estimate the number of asthma cases among PTBs.

Blomquist et al. (2011) used data from two surveys of U.S. adults to estimate annual WTP for asthma control for selected ages of children and adults. To account for children between ages 4 and 17, the applicable survey elicited parents’ values of controlling their children’s asthma. The survey reported WTP estimates for ages 4, 5, 8, 11, 15, and 17, and a linear interpolation between these values was used to value intervening years. These values were used to approximate the present value at birth of WTP for diagnosis of asthma at “school-age” by discounting the stream of annual WTP estimates from ages 4–17 back to age zero using a discount rate of 3%. The estimated net present value was \$38,541 per case.

2.2.3. Diabetes mellitus—Li et al. (2014) conducted a meta-analysis of PTB and both type 1 and type 2 diabetes mellitus (T1D and T2D, respectively) separately. A total of 18 studies for T1D were from the U.S., Canada, Europe, and Australia. The total five T2D studies include four studies from Europe (UK, Sweden, Finland, Denmark) and one from China, with various methods of outcome ascertainment ranging from self-report to physician diagnosis. Although for T2D there is uncertainty arising from the aforementioned traits of the study, this meta-analysis was still the most appropriate available at the time of the present study, and was deemed acceptable for use in the exploratory nature of this study. PTB was significantly associated with both T1D (OR = 1.18 (95% CI: 1.11, 1.25)) and T2D (OR = 1.51 (95% CI: 1.32, 1.72)). The respective ORs and prevalence of PTB, T1D, and T2D (Centers for Disease Control and Prevention, 2017) were used to estimate the number of cases of each diabetes type.

The American Diabetes Association (ADA) (2013) estimated annual costs per case of diabetes (type unspecified) of \$8,298 in direct medical costs and \$3,224 in reduced productivity costs. Reduced productivity costs were assumed to be additive to those calculated previously in this study, as those estimates were based on 1) the four DD's previously mentioned in the IOM report, and 2) IQ-related productivity. Costs of increased mortality from diabetes were only included in the form of productivity loss. Because approximately 95% of diabetes cases are T2D and approximately 5% are T1D, the cost estimates from the ADA were assumed to largely represent T2D costs and were therefore used to calculate benefits of reducing T2D cases. To derive an estimate of lifetime costs from the ADA's annual costs estimates, we assumed onset of T2D at age 50 and death at age 80—which were simplifying assumptions but generally consistent with conditional life expectancy at age 50 (United States Social Security Administration, 2018)—and discounted the resulting stream of costs back to birth at 3 percent. Lost workplace productivity costs were only included up to age 65. The estimated net present value was \$48,508 per case.

Tao et al. (2010) estimated expected lifetime medical costs and income loss from T1D in the U.S. by categories of age of onset from ages 3 to 45. To calculate present values, we assumed costs were uniformly distributed within the specified age categories (e.g., from 3–9 years old) and then discounted these age-specific costs to age zero. Summing these values across all ages of onset resulted in a net present value of \$199,313 of lifetime costs per case of T1D.

3. Results

3.1 Primary Analysis Results: Immediate Benefits

In 2008, there were 432,677 PTBs and 4,203,437 total births in the contiguous U.S., translating to a PTB rate of 0.103 (Table 2). The air quality data used for the baseline scenario, or before any simulated air quality change, indicated a nationwide range of county-level PM_{2.5} of 4.60 to 18.62 µg/m³, with a mean of 10.02 µg/m³ and median of 10.45 µg/m³ (Figure 1). The change in air quality from the simulated 10% decrease in county-level PM_{2.5} ranged from 0.46 to 1.86 µg/m³ across the states (Figure 2).

A hypothetical 10% reduction from baseline 2008 county-level PM_{2.5} levels was estimated to result in 5,016 fewer PTBs (1.16% of all PTBs) for a total of \$339 million of benefits nationwide (Table 3). The majority of benefits were from reduced medical costs, which constituted about \$251 million of the \$339 million of benefits. Numbers of reduced cases and associated benefits varied by state, with the percentage of PTB cases reduced from the simulated PM_{2.5} reduction ranging from 0.6 to 1.4% of the state's PTBs overall (Table 4). Sensitivity analyses of the lower and upper bounds of the reduced number of PTB cases resulted in 1,218 and 8,793 cases, respectively.

3.2. Supplemental Analysis Results: Additional Benefits

The previous estimate of 5,016 PTBs reduced was carried through to calculate the additional potential economic benefits from avoiding IQ decrements, asthma, T1D, and T2D cases. For this simulation, the greatest category of benefits was by far from the avoided IQ point decrements, which yielded an estimated \$669 million (Table 5). Sensitivity analyses using the lower and upper bounds of the mean weighted IQ decrement resulted in losses of 33,106 and 51,163 IQ points respectively, corresponding to \$526 million and \$813 million.

4. Discussion

PTB is an important health outcome for which epidemiological studies are increasingly finding associations with environmental contaminants. Estimates of the effects of a policy or risk management action on the incidence of PTB and the value of this change in incidence could be used to better inform decision-making. In this study, we explored an approach to quantifying the economic benefits of avoiding PTB and applied it to a simulated 10% reduction from 2008 PM_{2.5} levels. Mean ambient PM_{2.5} across the U.S. decreased by 22% from 2008 to 2015 (U.S. Environmental Protection Agency, 2017c), suggesting that the hypothetical 10% decrease was not an unrealistic air quality improvement to simulate. We found that the potential annual PTB benefits from reducing PM_{2.5} in our primary analysis may be in the order of hundreds of millions of dollars, possibly rising to over a billion dollars when also considering additional later-life health outcomes. For perspective, on a per-case-avoided basis, the estimated value of avoiding PTB (including later-life health outcomes) is greater than for other non-fatal PM_{2.5} health effects generally considered in EPA analyses except for chronic bronchitis (U.S. Environmental Protection Agency, 2017a).

EPA's most recent assessment of PM, published in 2009, determined that the evidence for PM_{2.5} and reproductive and developmental outcomes, a category that included PTB, was suggestive of a causal association (U.S. Environmental Protection Agency, 2009). The epidemiologic literature on this topic is much more extensive now than when the previous assessment was completed, and it is conceivable that the new PM_{2.5} assessment scheduled for completion in 2019 could determine that the weight of evidence is sufficient to conclude a likely causal or causal relationship between PM_{2.5} and PTB. If so, PTB would become a strong candidate for inclusion in future analyses of the benefits of PM_{2.5} reductions. However, even if the PM_{2.5} evidence concerning PTB is not judged to rise to a likely causal or causal weight-of-evidence determination, the analysis presented in this paper of the benefits of reduced PTB will be applicable to any other environmental contaminants that

may be found to have sufficient evidence. In either case, this type of benefits calculation would prove to be especially useful, as there is no existing WTP value for PTB, and the COI estimate in the IOM report, while useful, is dated and incomplete.

CDC WONDER reports data for continuous gestational age, and in theory, benefits could be estimated for changes in gestational age if 1) the PM_{2.5} epidemiological literature provided adequate effect estimates for gestational age as a continuous variable, and 2) sufficient evidence of causality was found in the weight-of-evidence determination of the relationship between PM_{2.5} and continuous gestational age. However, the binary variable was used in this study in accordance with the prevailing PM_{2.5} epidemiological literature available.

We used a two-step procedure to estimate the secondary outcomes reported in this study (IQ, asthma, T1D, and T2D), in which the first step was to compute the number of cases of PTB avoided, and the second step was to apply quantitative relationships from the literature regarding health consequences of PTB. The most recent PM ISA did not investigate the relationship between prenatal PM_{2.5} exposure and the secondary outcomes reported in this study. If there were direct evidence of a possible relationship between prenatal PM_{2.5} and IQ, asthma, T1D, or T2D, that evidence would be a primary consideration in a decision whether to include these secondary outcomes in a PM_{2.5} benefits analysis. In the absence of such direct evidence, it is reasonable to assume that the health consequences of PTB indicated in the literature are outcomes that would be avoided with any reduction in PTBs that results from lowered exposure to PM_{2.5}.

We estimated that 5,016 PTBs would have been avoided in 2008 with a 10% reduction in PM_{2.5}, resulting in \$339 million of immediate benefits and over \$669 million of additional health benefits. We have fairly high confidence in the estimate of PTBs avoided, conditional on the assumption that increased PM_{2.5} exposure increases the risk of PTB. The meta-analysis from which the PTB beta coefficient was derived, Sun et al. (2015), was the most comprehensive meta-analysis available at the time of our current study, and integrates estimates from many studies conducted in geographically diverse populations with a majority of studies from the U.S. The OR was 1.13 with a 95% confidence interval of 1.03 to 1.24, indicating to us with relatively strong confidence that there is a moderate and significant effect of PM_{2.5} on PTB, although the estimate is somewhat imprecise. However, there remains uncertainty regarding the exact nature and magnitude of the PM_{2.5}-PTB relationship, such as effects potentially varying by phase of gestation. For example, Sun et al. 2015 indicated statistically significant heterogeneity among studies, which subgroup and sensitivity analyses revealed to be due in part, but not entirely, to exposure assessment, study design, and study settings. Additionally, the literature regarding trimester-specific effects or predictive power remains mixed (Jalaludin et al., 2007; Lee et al., 2013; Sapkota et al., 2012; Selevan et al., 2000; Wilhelm and Ritz, 2005). The pooled estimate used in this study was from 13 studies of whole-pregnancy exposure, for which there were the greatest number of studies available and therefore the most statistical power. The effect estimates from the first, second, and third trimesters separately were almost identical, but fewer studies examined trimester-specific data (ten, five, and nine studies respectively), and all trimester-specific estimates were statistically insignificant. Thus, Sun et al. (2015) did not allow us to draw any strong conclusions regarding possible trimester-specific differences.

Another source of uncertainty in our analysis comes from the limited availability of comprehensive health and costs data. We used the IOM's estimates of the costs of PTB, which included limited medical costs, early intervention and special education costs, and lost wages, and adjusted these costs to 2014 dollars to derive a valuation estimate. However, the IOM's estimates did not include many later-life health, earnings, or education costs. For the purposes of our supplemental analysis, health and cost data were insufficient or not available for most potential later-life outcomes. We searched the literature to identify later-life outcomes associated with PTB and found many outcomes that had been studied, but most, such as cardiovascular disease or autism spectrum disorder, were not included in our analysis for one or more of the following reasons: 1) Low birth weight (LBW) was used as a proxy outcome for PTB in many earlier epidemiological studies. Evidence increasingly suggests that LBW and PTB, while overlapping, also have distinct etiologies and effects (Institute of Medicine, 2007). Therefore, we did not consider it appropriate to include studies conflating the two outcomes; 2) For many potential health outcomes of interest, evidence was not considered sufficient for quantification—there were no meta-analyses available to use for estimating incidence, only a few studies, mixed results, and/or results were statistically insignificant; 3) Some outcomes only had sufficient data for developing countries, which were assumed to differ greatly from the U.S., especially with regard to health care systems and economic outcomes; 4) The outcome definition differed between the health data and valuation data; and 5) Many outcomes simply lacked valuation estimates in the economics literature, even if they had epidemiologic evidence suitable for quantification. Among the outcomes we did include and value (IQ, asthma, T1D, and T2D), the body of literature regarding their relationship with PTB and their costs was not extremely comprehensive; additional research in these areas is expected to improve these estimates. The most robustly valued outcome was IQ, for which there could be uncertainty regarding the cost estimates used from Salkever, which have been debated in the literature (Grosse, 2007; Grosse et al., 2002; Robinson, 2007; Robinson, 2013; Salkever, 2014). However, based on methodological choices—for example, other studies did not consider work participation rates, demographic changes, or more recent data—Salkever's IQ-earnings estimates were deemed most appropriate for this study. Cost estimates for IQ were based on earnings, which are likely to underestimate WTP. However, among the four outcomes that were valued, IQ was still the dominant driver of costs; costs for the other three outcomes (asthma, T1D, and T2D) were relatively small.

Finally, there is uncertainty regarding the estimate used for the quantitative relationship between PTB and IQ. The population of infants in the Kerr-Wilson et al. (2012) study used to quantify this relationship was heavily skewed toward very or extremely preterm babies. As mentioned in the Methods section, because babies born preterm are on average moderately preterm (rather than very or extremely preterm), the moderately preterm category in Kerr-Wilson et al. (2012) was used over the binary preterm category to reduce possible overestimation of benefits that could result from including the higher costs associated with very preterm babies. The moderately preterm estimate compares mean IQ for births at gestational ages of 34 to 36 weeks to mean IQ for births at gestational ages of 37 weeks and greater. Depending on how our estimated decrease in PTB affects the overall distribution of PTB, using the moderately preterm category could still be an overestimate.

For the PTBs avoided from a reduction in $PM_{2.5}$, if we can assume that a child at any point of the preterm distribution can be re-assigned to any point of the term distribution, then a comparison of mean-to-mean costs for moderately preterm (which constitutes most preterm babies) and term babies is generally correct, and use of Kerr-Wilson et al. 2012's moderately preterm estimate should be accurate. However, if the simulated decrease in PTB results in a small but overall shift in the distribution of gestational ages, i.e. those right below the cutoff for term birth (very close to but not quite meeting 37 weeks) cross the somewhat arbitrary boundary for term birth (37 weeks and greater), then the average shift in gestational age may be much smaller than the shift underlying the Kerr-Wilson et al. (2012) estimate for moderately preterm births. This effect may occur because of differences by continuous gestational age within not only the moderately preterm category, but also the term category (e.g. outcomes may differ between babies born at 37 versus 40 weeks) (Noble et al., 2012). Regardless, no alternate value with less uncertainty in these respects was available, and we found utilizing the moderately preterm category from Kerr-Wilson to be a reasonable estimate given the current state of knowledge.

Our study is, to the best of our knowledge, the first study to simulate a decrease in $PM_{2.5}$ and subsequent decrease in $PM_{2.5}$ -related PTB, and to then quantify the PTB-related economic benefits arising from the simulated reduction in $PM_{2.5}$. Trasande et al. (2016) estimated the economic costs of all PTBs attributable to anthropogenic $PM_{2.5}$ exposure in 2010. $PM_{2.5}$ was assumed to be anthropogenic, rather than arising from natural sources such as wildfires, dust storms, or volcanoes, at levels above $8.8 \mu\text{g}/\text{m}^3$, a reference level which was originally applied in the 2010 Global Burden of Disease estimates of $PM_{2.5}$ -attributable disease (Lim et al., 2012). The OR of 1.15 (1.14, 1.16) from Sapkota et al. (2012), a meta-analysis which included 6 studies of the relationship between $PM_{2.5}$ and PTB, was utilized in the calculation of $PM_{2.5}$ -attributable PTB cases; conversely, we used the Sun et al. (2015) meta-analysis, which was more recent, included many more studies, and reports a slightly lower OR. Medical costs from birth to age 5 and costs after age 5 for developmental disabilities were obtained from the 2007 IOM report also used in the present study, and lost economic productivity was measured through IQ loss. Kerr-Wilson et al. (2012) was also used in Trasande et al. (2016); however, Trasande et al. used the 11.9-point IQ decrement between term babies and all preterm babies on average in the study, whereas we used the 8.4-point IQ decrement between term babies and moderately preterm babies for the reasons stated above. Trasande et al. did not include other later-life outcomes, such as those that we evaluated in our study (asthma, T1D, and T2D). Additionally, rather than using the Salkever estimates as we did, Trasande et al. used the estimates of changes in earnings per IQ point from Grosse et al. (2002), which are lower than the estimates proposed by Salkever (2014). They estimated 15,808 PTBs attributable to all $PM_{2.5}$ above $8.8 \mu\text{g}/\text{m}^3$ in 2010, with nationwide costs of \$5.09 billion (2010\$) for medical care costs and lost economic productivity combined. Although the Trasande et al. study was different in that it quantified economic costs of all $PM_{2.5}$ -attributable PTBs, while our study quantified costs for a fixed, simulated decrease in $PM_{2.5}$ and PTB, the two are consistent in indicating a high economic burden of PTB in the U.S.

Our study is also the first to utilize BenMAP to assess effects of prenatal exposures. BenMAP is used by EPA to perform benefits analyses of reductions in criteria pollutant

emissions and subsequent changes in incidence of health outcomes. Previously, its use was limited to health impacts on directly exposed populations; the capacity of BenMAP to evaluate health impacts of prenatal exposures provides potential for its use in a broader range of future benefits analyses. To illustrate our proposed approach, we applied a hypothetical scenario of a 10% reduction in $PM_{2.5}$ concentrations across the United States. As noted above, the concentration-response function is essentially linear, so the PTB cases avoided for alternate reductions in $PM_{2.5}$ concentrations is approximately proportional; for example, a uniform 5% reduction in $PM_{2.5}$ concentrations results in an estimated 2,515 PTBs avoided, or about half as many cases avoided as the 5,016 cases estimated for a 10% $PM_{2.5}$ reduction. In a benefits assessment of an actual policy measure, the relative reduction in $PM_{2.5}$ concentrations would vary across counties. BenMAP is well-suited to simulating varying reductions in pollutant concentrations associated with policy measures such as revisions to the NAAQS or sector-specific emissions controls. In addition, trends and projections in the U.S. fertility rate and PTB rate may affect the baseline number of PTB that would be affected by future policies to reduce $PM_{2.5}$ concentrations, and BenMAP is designed to easily incorporate such changes. A further refinement that could be implemented in assessment of actual policy measures would be to more fully consider sensitivity through the use of probabilistic uncertainty analysis, which is recommended in guidance from the Office of Management and Budget for federal regulations expected to have annual economic impacts of \$1 billion or more (Office of Management and Budget, 2003).

A principal benefit of this analytical approach is that it provides a straightforward way to estimate benefits in the absence of an existing WTP estimate for reduced risk of PTB. Because this method does not rely on an overarching WTP estimate for reduced PTB, the growing scientific knowledge base and new literature on specific PTB-related health outcomes can quickly be incorporated into calculations, allowing for direct revisions of benefits calculations based on the prevailing science. These qualities allow researchers and policymakers to obtain a broad overview of the health benefits of adverse environmental exposure reductions in a timely manner. A useful extension of this work would be to examine the distribution of these health benefits across the population by not only varying the changes in $PM_{2.5}$ across locations—for example, larger reductions in relatively more polluted areas to meet an air quality standard—but also to incorporate more localized incidence data and risk coefficients. While our analysis does incorporate county-level incidence, this may mask important heterogeneity within large counties, and we use a national-level risk coefficient. Our choices are appropriate for broad scale analyses of national policies, but may be less representative for more localized analyses (Hubbell et al., 2009).

The literature on environmental contaminants and birth outcomes is robust and growing (Bosetti et al., 2010; Ferguson and Chin, 2017; Grellier et al., 2010; Lamichhane et al., 2015; Li et al., 2017; Nieuwenhuijsen et al., 2013; Perera, 2017; Shah et al., 2011; Stillerman et al., 2008). Stieb et al. (2012), which analyzed multiple air pollution and birth outcomes in 62 studies by pollutant, outcome, and exposure period, already provides a foundation for potential future analyses for ozone, NO_2 , or SO_2 , which can be performed through BenMAP and for which BenMAP-compatible measurements can be obtained. In addition, specific health outcomes, such as high blood pressure (Parkinson et al., 2013), have

suggested or established relationships with PTB, and may therefore hold promise for future valuation estimates. This type of study could be undertaken to quantify economic effects of pollutant-related health outcomes currently unquantified in BCAs, which can contribute to more comprehensive analytical underpinnings of future decision-making.

5. Conclusions

Although PTB is an important health outcome with both short- and long-term consequences that may yield significant economic costs, there is not a robust body of economic literature to support an estimate of the WTP to reduce its risk. There is a need to develop methodologies and estimates that can provide information regarding the potential benefits of reducing such detrimental health outcomes. The analysis presented here of PTB and PM_{2.5} indicate that previously unquantified benefits of reducing pollution-related cases of health outcomes may be substantial and are worthy of investment for future research. Further research that would likely reduce the uncertainty in important elements of our analysis include: updated meta-analysis of the PM_{2.5}-PTB relationship, which can be expected to provide a more precise effect estimate as the total sample size is increased; and an updated estimate of the incremental medical costs associated with PTB and/or a study of parents' WTP to avoid PTB. In addition, further research on the consequences for adult health of being born preterm may identify additional effects that should be incorporated into PTB benefits analysis, or may change effect estimates for outcomes included in this analysis with relatively small estimated benefits (i.e. asthma and diabetes).

Acknowledgements

We thank Neal Fann, US EPA, for his guidance and assistance with BenMAP, and Charles Griffiths, US EPA, for his valuable feedback and review of an earlier draft of this paper.

Funding: This work was supported by the Cooperative Agreement Number X3-83555301 between the U.S. Environmental Protection Agency and the Association of Schools and Programs of Public Health during the first author's ASPPH Environmental Health Fellowship at the National Center for Environmental Economics, Office of Policy. The views expressed in this publication are those of the authors and do not necessarily represent the official views or policies of the EPA or ASPPH.

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Figure 1.
Distribution of baseline county-level PM_{2.5} annual mean concentrations in the U.S. in 2008.

Figure 2.
Changes in county-level PM_{2.5} levels ($\mu\text{g}/\text{m}^3$) after a simulated 10% decrease from baseline 2008 levels.

Table 1.

Summary of PTB costs as derived from IOM report (Institute of Medicine, 2007).

Cost categories	Average incremental costs per PTB (2005\$)	Index used to update IOM estimate to 2014\$
Medical costs associated with: • Maternal delivery • Birth to age 5 years • Cerebral palsy, intellectual disability, vision impairment, and hearing loss (4 DDs)	\$37,022	Medical costs
Early intervention Special education (4 DDs)	\$3,353	All goods
Lost productivity (4 DDs)	\$11,214	Wages
Total	\$51,589	-

Table 2.

Baseline scenario of preterm birth rates in the contiguous U.S. with no reduction in ambient PM_{2.5} in 2008.

	All U.S.
Baseline PTBs (n)	432,677
Baseline All Births (n)	4,203,437
PTB Rate	0.103

Table 3.

National changes in cases of preterm birth and associated economic benefits after a simulated 10% decrease in PM_{2.5} from baseline 2008 levels (2014\$).

Reduced PTB cases (n)	5,016
Benefits from reduced PTB (2014\$ millions)	\$339.1
Medical costs	\$250.7
Special education costs	\$ 20.4
Lost productivity	\$ 68.1

Table 4.

State-level changes in cases of preterm birth and associated economic benefits after a simulated 10% decrease in PM_{2.5} from baseline 2008 levels.

State	Baseline PTB Cases (n)	Reduced PTB Cases (n)	PTB Case Reduction (%)	Benefits from Reduced PTB (2014\$ millions)
Alabama	8,263	102	1.2%	\$6.9
Arizona	10,038	117	1.2%	\$7.9
Arkansas	4,705	56	1.2%	\$3.8
California	48,992	620	1.3%	\$41.9
Colorado	6,679	51	0.8%	\$3.5
Connecticut	4,056	47	1.2%	\$3.2
Delaware	1,212	16	1.3%	\$1.1
District of Columbia	1,090	14	1.2%	\$0.9
Florida	25,623	211	0.8%	\$14.2
Georgia	16,987	213	1.3%	\$14.4
Idaho	2,342	20	0.8%	\$1.3
Illinois	18,229	235	1.3%	\$15.9
Indiana	9,369	125	1.3%	\$8.4
Iowa	3,906	43	1.1%	\$2.9
Kansas	3,845	40	1.0%	\$2.7
Kentucky	6,832	88	1.3%	\$5.9
Louisiana	8,163	85	1.0%	\$5.8
Maine	1,176	10	0.9%	\$0.7
Maryland	8,399	107	1.3%	\$7.2
Massachusetts	6,694	72	1.1%	\$4.9
Michigan	12,680	148	1.2%	\$10.0
Minnesota	6,343	66	1.0%	\$4.5
Mississippi	6,082	71	1.2%	\$4.8
Missouri	8,283	98	1.2%	\$6.6
Montana	1,240	10	0.8%	\$0.7
Nebraska	2,574	24	0.9%	\$1.6
Nevada	4,310	43	1.0%	\$2.9
New Hampshire	1,142	11	1.0%	\$0.7
New Jersey	11,779	142	1.2%	\$9.6
New Mexico	2,933	19	0.6%	\$1.3
New York	23,906	280	1.2%	\$18.9
North Carolina	13,984	172	1.2%	\$11.7
North Dakota	875	7	0.8%	\$0.5
Ohio	15,871	217	1.4%	\$14.6
Oklahoma	6,026	70	1.2%	\$4.7

State	Baseline PTB Cases (n)	Reduced PTB Cases (n)	PTB Case Reduction (%)	Benefits from Reduced PTB (2014\$ millions)
Oregon	3,847	37	1.0%	\$2.5
Pennsylvania	15,126	202	1.3%	\$13.6
Rhode Island	1,186	12	1.0%	\$0.8
South Carolina	7,405	89	1.2%	\$6.0
South Dakota	1,037	9	0.9%	\$0.6
Tennessee	9,743	117	1.2%	\$7.9
Texas	45,246	508	1.1%	\$34.4
Utah	5,387	54	1.0%	\$3.6
Vermont	529	5	0.9%	\$0.3
Virginia	11,151	135	1.2%	\$9.1
Washington	7,940	80	1.0%	\$5.4
West Virginia	2,540	34	1.3%	\$2.3
Wisconsin	6,091	79	1.3%	\$5.3
Wyoming	821	6	0.7%	\$0.4
U.S. Range	529 – 48,992	5 – 620	0.6 – 1.4%	\$0.3 – 41.9

Table 5.

Additional benefits from avoided later-life health outcomes of preterm birth after a simulated 10% decrease in PM_{2.5} from baseline 2008 levels.

	n (IQ points or Cases)	Benefits per n (2014\$)	Total Benefits Estimate (2014\$ millions)
IQ	42,134 IQ points	\$15,884	\$669.3
Asthma	160 cases	\$35,272	\$5.6
Type 1 Diabetes	4 cases	\$199,313	\$0.8
Type 2 Diabetes	190 cases	\$48,508	\$9.2