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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 relationship between a mother's exposure to air pollution 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 a potential approach to assess 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 and county-level air quality and PTB data to estimate the potential health and economic benefits of a reduction in air pollution-related PTB, with fine particulate matter ($PM_{2.5}$) as our case study pollutant. Using this method, a simulated 10% decrease from 2008 $PM_{2.5}$ levels resulted in a reduction of 5,016 PTBs and savings of at least $339 million, potentially reaching over one billion dollars when considering later-life effects of PTB.

KEYWORDS: air pollution, preterm birth, benefits, $PM_{2.5}$

JEL CODES: D61, I18, J13, Q51, Q53

Preterm Birth and Economic Benefits of Reduced Maternal Exposure to Fine Particulate Matter[*†]

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Introduction

Preterm birth (PTB), or birth before 37 weeks of gestation, is a leading predictor of infant mortality [1] and an important contributor to later-life disease and disability [2]. Prior analysis suggests that the relatively high rate of infant mortality [3] in the United States (U.S.) may largely be due to a high PTB rate, and decreasing the PTB rate could thereby significantly reduce infant mortality in the U.S. [4]. 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 [2].

A growing body of evidence suggests a relationship between a mother's exposure to environmental contaminants during pregnancy and PTB of her baby [5-7]. The most extensive evidence of this relationship is for ambient air pollution. "Criteria air pollutants" are six pollutants —carbon monoxide, lead, nitrogen dioxide, ozone, particulate matter (PM), and sulfur dioxide—commonly found across the U.S. for which the Clean Air Act requires the U.S. Environmental Protection Agency (EPA) to set National Ambient Air Quality Standards (NAAQS).

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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 [8-12]. The potential relationship between 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 is placed on individuals in disadvantaged communities, who are already subjected to multiple socioeconomic and health inequities.

Regulations promulgated under the Clean Air Act to limit or reduce exposure to criteria pollutants are subject to many requirements by statute, executive order (EO), and EPA policy. Though benefit-cost analysis (BCA) for setting primary 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. As such, BCA has typically been conducted when setting primary NAAQS and for other economically significant rulemakings affecting emissions of 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. 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 reduction in risk to one's health.

In principle, WTP is comprehensive measure that reflects the full set of health outcomes associated with a reduction in risk, but many health effects, including PTB, lack an estimate of WTP in the economics literature[5]. An alternative 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 [13]. However, few studies exist on the economic costs of PTB, particularly those considering costs past the neonatal time period. These issues hinder identifying and adopting the most efficient or cost-effective policies and have been recognized by the Institute of Medicine[6] (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, reported that the evidence for reproductive and developmental outcomes overall, including PTB, low birth weight, birth defects, and infant mortality, was suggestive of a causal relationship. However, the limited studies specifically examining fine particulate matter ($PM_{2.5}$) and PTB mostly reported statistically significant positive associations [8]. Newer studies of $PM_{2.5}$ and PTB published since 2008 will be considered in an updated ISA that is projected to

[5] More details are available in EPA's *Guidelines for Preparing Economic Analyses*, Chapter 7: Analyzing Benefits (EPA, 2010).

[6] The IOM is now called the Health and Medicine Division of the National Academies of Sciences, Engineering, and Medicine.

be completed in 2019 [14]. 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 is widespread human exposure to them, indicating high potential benefits of reducing PTB associated with criteria pollutant 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.

Methods

Overview. Quantification of $PM_{2.5}$-attributable PTB reduction and associated economic benefits entailed the following:

1) Calculation of the reduction in number of PTB cases attributable to a chosen air quality improvement via decreased ambient $PM_{2.5}$ levels; and

2) Valuation (monetization) of immediate and later-life consequences of the PTB cases derived above.

Primary Analysis: 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 the contiguous U.S.[7] and enables translation of a health effect estimate into risk per increment of exposure. This study utilized BenMAP to estimate the potential PTB benefits of a reduction of ambient concentrations of county-level $PM_{2.5}$ nationwide.

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.

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

[7] Because BenMAP does not include data for Alaska or Hawaii, this analysis is for the contiguous U.S. Any mention of U.S. or national data or analyses in this paper hereafter refers to the contiguous U.S.

Health impact and valuation results were first calculated at the county level and then aggregated to provide state-level and national estimates.

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 [15]. The VNA method calculates an inverse-distance weighted average of the monitors surrounding a county's center to represent the county's overall $PM_{2.5}$ level[8] [16, 17]. $PM_{2.5}$ 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[9] in 2008 annual average county-level $PM_{2.5}$ concentrations across the country [18].

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 [19]. 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 [20]. Multiplying the population of women ages 15 to 44 by fertility rate yielded a unit of all births[10], 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.

[8] Predicted estimates tend to be less reliable in rural or remote areas due to fewer monitors being present. These data inherently represent smaller populations with few to no alternative measurements available, and measurement error is expected to be negligible for the purposes of this study.

[9] Mean ambient $PM_{2.5}$ across the U.S. decreased by 21.7% from 2008 to 2015, indicating that a simulated 10% decrease is not an unrealistic air quality improvement.

[10] Using this calculation, rather than obtaining separate data on all births specifically, is beneficial for analyses that may involve future projections of benefits.

Baseline prevalence rates. The numbers of PTBs and all births in each county were obtained from CDC WONDER[11] for 2008. County-level baseline prevalence rates ($\boldsymbol{y_0}$) were calculated as all PTBs[12] 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[13].

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. [7] 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 μg/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 μg/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 = 1.03, 1.24). We converted the central estimate of this pooled OR to a logistic regression β coefficient of 0.012

[11] Wide-ranging Online Data for Epidemiologic Research

[12] CDC WONDER has data for continuous gestational age, but the binary variable was used in this study in accordance with the prevailing $PM_{2.5}$ epidemiological literature available.

[13] Unidentified Counties rates rather than statewide rates were used in counties with suppressed data under the assumption that unidentified counties would be more similar to counties with suppressed data, as both have smaller, less dense populations. Any possible measurement error from this assumption is expected to be minimal, as these data inherently represent much smaller populations.

relating risk per 1 μg/m^3 increase in $PM_{2.5.}$ by using the general formula $\boldsymbol{ln(OR) = \beta \cdot \Delta PM_{2.5}}$ as illustrated in the BenMAP User Manual Appendices [21].

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, no such estimates exist 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.

Table 1. Summary of PTB costs as derived from IOM report.

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	-

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 [2]. 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.

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 for most post-neonatal health outcomes, effects on familial dynamics, or earnings and education in the U.S. 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 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.

Cognitive benefits: IQ. Kerr-Wilson et al. 2012 [22] 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 $\geq$32 weeks vs. term) and IQ deficits. The meta-analysis included 27 studies of 7,044 children total. The average gestational age of the pre-term 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 (6.6, 10.2) points lower than that of term babies.

EPA has routinely valued the benefits of avoided IQ decrements[14] 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 [23] of this model, EPA derived average lifetime earnings values from U.S. Census data and used Salkever et al. 1995's [24] estimates[15] [25, 26] to calculate an economic cost of $15,884 for each IQ point loss.

Asthma. Sonnenschein-van der Voort et al. 2014 [27] 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[16] cohorts. The meta-analysis reported a pooled OR of 1.40 (1.18, 1.67). This OR and the prevalence of PTB and asthma [28] were used to estimate the number of asthma cases among PTBs.

Blomquist, Dickie, and O'Conor 2011 used data from two surveys to estimate annual WTP for asthma control for selected ages of children ranging from 4-17. 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-

[14] The present IQ valuation is not expected to overlap with costs of reduced work productivity previously included in the IOM estimates, which account for labor market participation rates, disability-specific work limitation, and earnings losses associated with limitations. The potential for slight overlap with regards to the 4 DD's is recognized; however, they are relevant to a small portion of total PTBs, and any possible overlap is expected to be negligible.
[15] EPA also uses Schwartz 1994 estimates, which yield a cost per IQ point of $11,559. However, Salkever 1995 was re-examined in 2014 and was deemed to be better suited for the present analysis.
[16] It was assumed that incorporating studies of European populations in the present analysis would not produce appreciable problems arising from non-generalizability, as the health relationships of interest were not believed to be related largely to cultural or national differences.

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.

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 (1.11, 1.25)) and T2D (OR = 1.51 (1.32, 1.72)). The respective ORs and prevalence of PTB, T1D, and T2D [29] were used to estimate the number of cases of each diabetes type.

The American Diabetes Association (ADA) estimated annual costs per case of diabetes (type unspecified) of $8,298 in direct medical costs and $3,224 in reduced productivity costs[17]. 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 annual costs estimates, we assumed onset of T2D at age 50, death at age 80[18], and

[17] 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.

[18] This is a simplifying assumption but generally consistent with conditional life expectancy at age 50 (https://www.ssa.gov/oact/STATS/table4c6.html). Lost workplace productivity costs are only included up to age 65.https://www.ssa.gov/oact/STATS/table4c6.html).

discounted the resulting stream of costs back to birth at 3 percent. 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.

Results

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 $\mu g/m^3$, with a mean of 10.02 $\mu g/m^3$ and median of 10.45 $\mu g/m^3$ (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 $\mu g/m^3$ across the states (Figure 2).

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

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

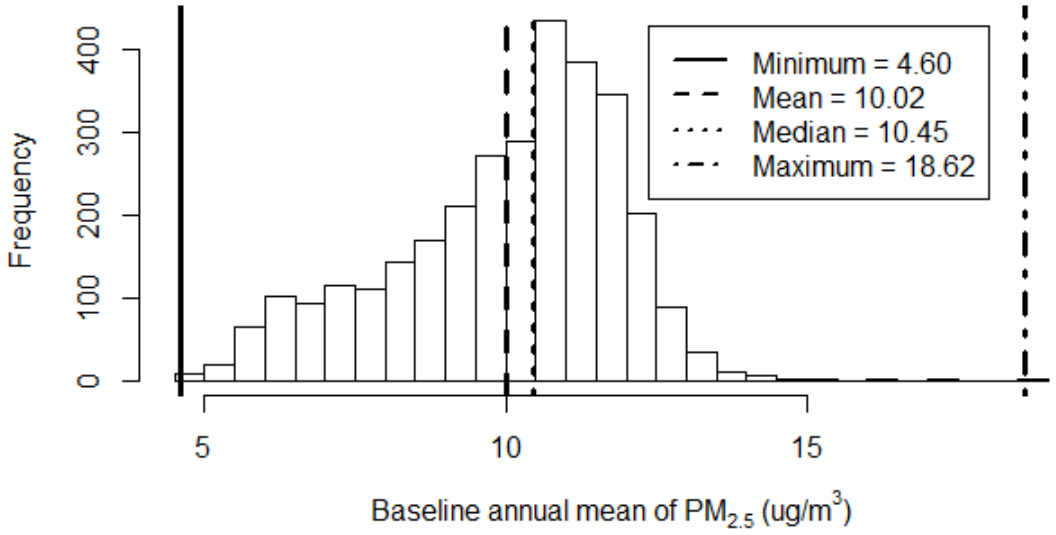
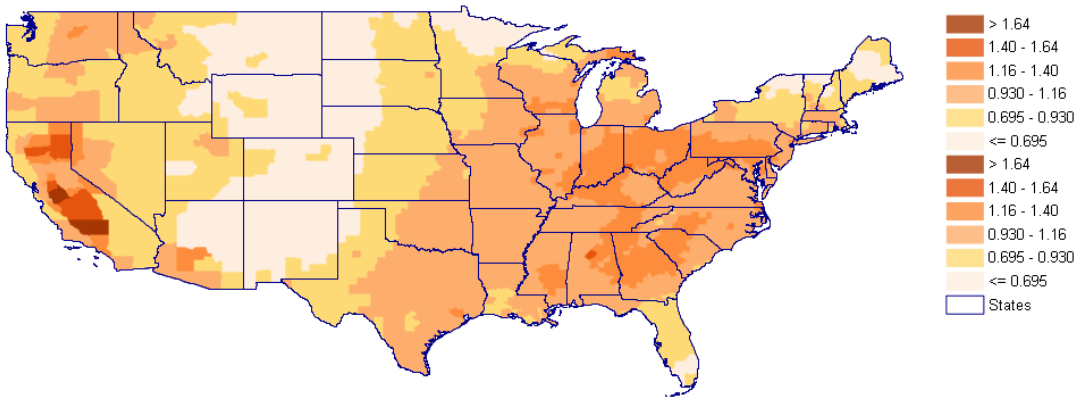


Figure 2. Changes in county-level $PM_{2.5}$ levels (µg/m^3) after a simulated 10% decrease from baseline 2008 levels .



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 PTBs) for a total of $339 million of benefits nationwide (Table 3). The majority of benefits were from medical costs, which constituted about $251 million of the $339 million of benefits overall in the primary analysis. 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).

Table 3. National changes in preterm birth cases and associated economic benefits after a simulated 10% decrease in $PM_{2.5}$ from baseline 2008 levels (2014$).

Reduced PTB Cases (n)	5016
Benefits from Reduced PTB (2014$ millions)	$339.1
Special Education Costs	$20.4
Medical Costs	$250.7
Lost Wages	$68.1

Table 4. State-level changes in preterm birth cases 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
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

Supplemental Analysis Results: Additional Benefits

The previously calculated 5,016 PTBs 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).

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$)	Total Benefits Estimation (2014$ 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

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 hypothetical reduction in $PM_{2.5}$. 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 value of 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 [30]. 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. 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[19] 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.

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 of prenatal $PM_{2.5}$ with 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

[19] In theory, benefits could be estimated for changes in gestational age if 1) the $PM_{2.5}$ epidemiological literature provided adequate effect size 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.

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. 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 [31-35]. 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. In our primary analysis, 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 [2]. 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) For some outcomes, 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 [26, 36-39]. 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 enter 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. 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) [40]. 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 [41]. $PM_{2.5}$ was assumed to be anthropogenic, rather than arising from natural sources such as wildfires, dust storms, or volcanoes, at levels above 8.8 $\mu g/m^3$, a reference level which was originally applied in the 2010 Global Burden of Disease estimates of $PM_{2.5}$-attributable disease [42]. The OR of 1.15 (1.14, 1.16) from Sapkota et al. 2012 [34], 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 reports a slightly lower OR, as it was more recent and included many more studies. 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 preterm babies on average in the study, whereas we used the 8.4-point IQ decrement between term babies and moderately preterm babies for 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 [36]. They estimated 15,808 PTBs attributable to $PM_{2.5}$ 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 reduction of 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.

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.

The literature on environmental contaminants and birth outcomes is robust and growing [5, 43-50]. Stieb et al. 2012, which analyzed multiple air pollution and birth outcomes in 62 studies by pollutant, outcome, and exposure period[20], 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 [6]. In addition, specific health outcomes, such as high blood pressure [51], 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.

[20] Sun et al. 2015 was used in the analysis over Stieb et al. 2012 because the latter included only six studies measuring the $PM_{2.5}$-PTB association.

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.

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