Traffic related air pollution and the burden of childhood asthma in the contiguous United States in 2000 and 2010

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Background: Asthma is one of the leading chronic airway diseases among children in the United States (US). Emerging evidence indicates that Traffic Related Air Pollution (TRAP), as opposed to ambient air pollution, leads to the onset of childhood asthma. We estimated the number of incident asthma cases among children attributable to TRAP in the contiguous US, for the years 2000 and 2010.

Methods: The number of incident childhood asthma cases and percentage due to TRAP were estimated using standard burden of disease assessment methods. We combined children (<18 years) counts and pollutant exposures at populated US census blocks with a national asthma incidence rate and meta-analysis derived concentration response functions (CRF). NO2, PM2.5 and PM10 were used as surrogates of TRAP exposures, with NO2 being most specific. Annual average concentrations were obtained from previously validated land-use regression (LUR) models. Asthma incidence rate and a CRF for each pollutant were obtained from the literature. Estimates were stratified by urban or rural living and by median household income. We also estimated the number of preventable cases among blocks that exceeded the limit for two counterfactual scenarios. The first scenario used the recommended air quality annual averages from the World Health Organization (WHO) as a limit. The second scenario used the minimum modeled concentration for each pollutant, in either year, as a limit.

Results: Average concentrations in 2000 and 2010, respectively, were 20.6 and 13.2 μg/m3 for NO2, 12.1 and 9 μg/m3 for PM2.5 and 21.5 and 17.9 μg/m3 for PM10. Attributable number of cases ranged between 209,100–331,200 for the year 2000 and 141,900–286,500 for 2010, depending on the pollutant. Asthma incident cases due to TRAP represented 27%–42% of all cases in 2000 and 18%–36% in 2010. Percentage of cases due to TRAP were higher (1) in urban areas than rural areas, and (2) in block groups with lowest median household income. Online open-access interactive maps and tables summarizing findings at the county level and 498 major US cities, are available at [https://carteehdata.org/l/s/TRAP-burden-of-childhood-asthma]. Assuming that pollutants did not exceed WHO air quality recommendations, the number of incident cases that could have been prevented ranged between 300 and 53,400, depending on the pollutant and year. Assuming that pollutant levels were limited to the minimum modeled concentration, then the number of childhood asthma incident cases that could have been prevented ranged between 127,700 and 317,600, depending on the pollutant and year.

Conclusion: This is the first study to estimate the burden of incident childhood asthma attributable to TRAP at...
1. Introduction

Asthma is the reversible or partially reversible obstruction of airflow presenting as episodes of wheezing, cough and shortness of breath with varying degrees of severity (National Heart Lung and Blood Institute, 2007). Globally, there are $>334$ million people affected by asthma (Global Asthma Network, 2014). In the United Stated (US) alone, $>8\%$ of adults and children had ongoing asthma during 2016, which translated to 20 million adults and 6 million children, making asthma the most common chronic lung disease among children (Zahran et al., 2018). US survey studies conducted between 2006 and 2010 showed that 60% of children with current asthma had some form of persistent asthma either being on long-term control medications or having uncontrolled asthma (CDC, 2010).

The economic and educational burden of asthma is great. According to the Centers for Disease Control and Prevention (CDC), each year, asthma results in more than $56$ billion in health care costs in the US (CDC, 2010). A study by Nurmagambetov et al. (2018) estimated that the total combined economic burden of asthma from missed work and school days, medical costs and mortality in 2013 in the US amounted to $81.9$ billion. In 2008 alone, there was an estimated 10.4 million missed school days for children with asthma, which also led to missed work days among children’s caregivers (CDC, 2010). Nurmagambetov et al. (2018) also stated that annual spending on prescription medication, office-based visits, outpatient visits, emergency room visits and inpatient hospital admissions averages $1700$ more for families with (compared to without) asthmatic children (<18 years).

Asthma is a heterogeneous disease with multiple sub-phenotypes and different pathological, biological and clinical characteristics (Gowers et al., 2012; Wenzel, 2012). The increasing understanding of the complex causal pathways of asthma where environmental and genetic factors interact has led to the discovery of these multiple sub-phenotypes. However, causal pathways are still not completely understood (Martinez, 2007). Air pollution, an environmental factor that is well known to exacerbate pre-existing asthma, was believed not to lead to the onset of new cases of the disease (Kryzanowski and Cohen, 2008; WHO, 2005; Anderson et al., 2011). However, emerging evidence indicates that specific mixtures/types of air pollutants are associated with asthma onset, more specifically Traffic Related Air Pollution (TRAP), challenging prior belief that air pollution does not contribute to asthma development. Traffic emits a wide range of pollutants through combustion and non-combustion routes and is a major source of urban air pollution. Several factors contribute to the type and quantity of pollutants emitted including vehicle type, age, condition, fuel type and road type. Combustion pollutants include carbon monoxide (CO), Nitrogen oxides (NOx), particulate matter (PM), benzene, lead, Sulphur, secondary by-products and aerosols (e.g. ozone, and nitrates) and others, while non-combustion pollutants (i.e. tire wear, brake wear and resuspended dust) include organic materials (e.g. n-alkanoic acids and various polymers), carbonaceous material, heavy metals and other chemicals. Exposure to pollutants from both emissions is known to cause a wide range of adverse health effects. To estimate the health effects of the TRAP mixture, epidemiological studies use two broad categories as surrogates of traffic exposure: (1) Estimating a buffer zone of exposure by measuring the distance to road or traffic density and (2) Modeling/measuring concentrations of pollutants or of traffic related pollutants, mainly NO2, elemental carbon (EC) or Black Carbon (BC), PM, benzene, and ultrafine particles (UFP) (Health Effects Institute, 2010). NO2 and BC are considered better traffic surrogates compared to PM2.5 and PM10 which are less specific to the TRAP mixture and have numerous other biogenic and anthropogenic sources (Richmond-Bryant et al., 2009; Anderson et al., 2013; Khreis et al., 2017).

A meta-analysis by Anderson et al. (2013) examined 17 cohorts that analyzed long term exposure to air pollution and development of asthma, and found that exposure to NO2, but not PM2.5, was significantly associated with asthma incidence in both children and adults. More recently, Khreis et al. (2017) examined 41 papers that included case-control, cross-sectional and cohort studies and that studied the associations between incident childhood asthma and exposure to TRAP and traffic surrogates. The authors concluded that intra-urban BC, NO2, PM2.5 and PM10 were all statistically significantly associated with asthma incidence. These associations remained significant even after the exclusion of case-control and cross-sectional studies from the analyses. A more recent study examining the development of asthma with early life exposure to NO2 at the census block level in the US also found that with each interquartile increase in concentration, the odds ratio for developing asthma was 1.25 (95% CI = 1.10–1.41) for NO2 and 1.25 (95% CI = 1.06–1.46) for PM2.5 (Kravitz-Wirtz et al., 2018).

Although there is now convincing evidence linking TRAP with childhood asthma incidence, few studies have examined the burden of asthma attributable to TRAP. A study of 10 European cities, where on average 31% of the combined population lived within 75 m of high traffic volume roads, reported that proximity to major roadways accounted for 14% of all childhood asthma cases (Perez et al., 2015). In the US, a study in Southern California examining exposure to air pollution from major roads and ship emissions and using an 8-year average concentration of NO2 and Ozone (O3) found that up to 9% of childhood asthma cases could have been prevented if exposures were reduced to levels found in clean communities (Perez et al., 2009). To our knowledge, no study focused on the burden of childhood asthma attributable to TRAP nationally in the US and the spatial coverage of previous studies was limited.

In this study, we aim to estimate the number of incident childhood asthma cases attributable to TRAP for the whole contiguous US. For this purpose, we use NO2, PM2.5 and PM10 concentrations as surrogates of the TRAP mixture across all populated US census blocks for years 2000 and 2010. NO2 is a more specific traffic marker and represents the main analysis of this paper while the PM analyses are considered ancillary analyses, less specific to, and likely overestimating the contribution of traffic sources. We also compare the change in burden between the two decennial years.

2. Methods

2.1. Study area and time points

We analyzed data for the contiguous US (48 states and District of Columbia) for the years 2000 and 2010 at the census block level (the smallest available geographical unit for census data). One variable of interest, the median household income, was only available at the census block group level, which is one geographical level higher than the census block (US Census Bureau, 2010). Only populated census blocks were included in our analyses. We selected years 2000 and 2010 owing to: 1) the availability of full population counts from the decennial census, and 2) the availability of exposure estimates at a geographical level matching the census block level for the contiguous US. Air pollution data were unavailable for Alaska, Hawaii or Puerto Rico, and hence they were excluded from our analysis.
2.2. Census data

We obtained the decennial census data for 2000 and 2010 from the National Historical Geographic Information System (NHGIS) website (Manson et al., 2017). The data included total population counts and total counts of children <18 years old living in the contiguous US at the census block level, the smallest geographical units used by the US Census Bureau to collect and tabulate decennial census data (US Census Bureau, 1994). For our study, we only included populated census blocks. Population counts were stratified into urban or rural at the census block level, while annual median household income was stratified into: < $20,000, $20,000 to < $35,000, $35,000 to < $50,000, $50,000 to < $75,000 and ≥ $75,000, at the census block group level – not adjusted for inflation. There were 2686 (0.04%) census blocks with missing median income data in 2010 and these were excluded from the analysis.

Table 1 provides a summary of demographic and geographic characteristics in census blocks for both years. The total number of children in 2000 was 71,807,328 (26% of the total population) and in 2010 was 73,690,271 (24% of the total population). By living location, 79% and 81% of children lived in an urban setting in 2000 and 2010, respectively. By median household income, fewer children lived in the lowest median income group compared to other groups across both years (not adjusted for inflation).

2.3. Asthma incidence and prevalence estimation

US national asthma incidence rates for children in 2000 and 2010 were not readily available. However, for the purpose of our analysis, we used an aggregated annual average asthma incidence rate of 12.5 (95% CI = 10.5–14.4) per 1000 at-risk children for the period 2006–2008 extracted from 31 states and the District of Columbia with a total sample size of 8437 children from the ACBS and 200,993 from the BRFSS, as published by Winer et al. (2012). This asthma incidence rate was estimated using the Behavioral Risk Factor Surveillance System (BRFSS) and the Asthma Call-Back Survey (ACBS) data sets (CDC, 2009; CDC, 2011). Both surveys were conducted by the CDC and are described next.

The BRFSS is a continuous national health-related telephone survey conducted in all 50 states as well as the District of Columbia and the three US territories (Guam, Puerto Rico and Virgin Islands). The ACBS is a follow-up survey in participating states among select individuals with an affirmative asthma diagnosis, as established during the BRFSS.

If states participate in an optional random child selection module, an adult respondent may serve as a proxy for one randomly selected child (<18 years) per household (CDC, 2009). To estimate the childhood asthma incidence rate, participants were assessed for a “lifetime asthma” status obtained through the BRFSS question: “Has a doctor, nurse, or other health professional ever said that the [name of child] has asthma?” If the answer is “yes”, the respondent is then asked to participate in the ACBS. If the respondent answered “no”, the child is designated the status “never asthma”. During the follow-up ACBS interview, the respondent is then asked “How old was the [name of child] when a doctor or other health professional first said [he/she] had asthma? How long ago was that?” If the answer is “within the past 12 months”, the child is designated the status “newly diagnosed asthma case”.

Asthma incidence rate was estimated as the number of newly diagnosed asthma cases, within a specified time period, among at-risk children. At-risk children are the sum of “never asthma” and “newly diagnosed asthma cases” among children (i.e. excluding prevalent cases in each year). Fig. 1 shows a flow chart of how asthma incident cases were ascertained through the BRFSS and ACBS (Winer et al., 2012). The asthma prevalence rate was 12.4% and 13.7% for the years 2000 and 2010, respectively, which was obtained from the Summary Health Statistics for US Children: National Health Interview Survey report for each corresponding year (Blackwell et al., 2003; Bloom et al., 2011).

2.4. Exposure assessment models and data sets

We estimated the annual average concentrations in μg/m³ for NO₂, PM₂.₅ and PM₁₀ for the years 2000 and 2010 at the centroid of all included census blocks. NO₂ concentrations were converted from ppb to μg/m³ through multiplying by 1.88 (WHO, 2005). Table 2 provides a detailed summary of pollutant concentrations across both years. Pollutant data at the state level and across the different strata (urban versus rural and by median household income) are provided in Fig. S1–S2 and Table S1–S2.

2.4.1. NO₂ models

The NO₂ estimates were obtained from a land-use regression (LUR) model, developed by, and described in detail in Bechle et al. (2015). In brief, the model uses satellite data and Environmental Protection Agency (EPA) air quality monitor readings of NO₂ concentrations alongside several covariates (for example, impervious surfaces, elevation, major roads, residential roads, and distance to coast) to estimate
NO\textsubscript{2} concentrations. The model also incorporates temporal scaling by estimating average monthly monitor readings for 11 consecutive years. The final model used has a relatively high predictive power at unmeasured locations which was tested using a hold-out cross validation with good model performance (R\textsuperscript{2} = 0.82); which is comparable with other continental-scale NO\textsubscript{2} LUR models (Beelen et al., 2009; Hystad et al., 2011; Novotny et al., 2011; Vienneau et al., 2013). The population-weighted average NO\textsubscript{2} concentration in the US decreased from 20.6\,μg/m\textsuperscript{3} in 2000 to 13.2\,μg/m\textsuperscript{3} in 2010 (Table 2).

**Table 2**

Summary of pollutant concentrations using populated census blocks only.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>NO\textsubscript{2} μg/m\textsuperscript{3}</th>
<th>PM\textsubscript{2.5} μg/m\textsuperscript{3}</th>
<th>PM\textsubscript{10} μg/m\textsuperscript{3}</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2000</td>
<td>2010</td>
<td>Change (%)</td>
</tr>
<tr>
<td>Mean</td>
<td>20.6</td>
<td>13.2</td>
<td>−36%</td>
</tr>
<tr>
<td>Min</td>
<td>2.2</td>
<td>1.5</td>
<td>−32%</td>
</tr>
<tr>
<td>25%</td>
<td>12.1</td>
<td>7.9</td>
<td>−35%</td>
</tr>
<tr>
<td>50%</td>
<td>17.9</td>
<td>11.4</td>
<td>−36%</td>
</tr>
<tr>
<td>75%</td>
<td>26.3</td>
<td>16.6</td>
<td>−37%</td>
</tr>
<tr>
<td>Max</td>
<td>95.9</td>
<td>58.3</td>
<td>−39%</td>
</tr>
</tbody>
</table>
2.4.2. PM$_{2.5}$ and PM$_{10}$ models

Annual average concentrations were estimated using data from 17 years (1999–2015) for PM$_{2.5}$ and 27 years (1988–2015) for PM$_{10}$. The data were derived from regulatory monitors and estimates were constructed in a universal kriging framework (Kim et al., in prep). Partial least squares were estimated for model performance from hundreds of geographic variables, including land use, population, and satellite-derived estimates of land use and air pollution. Hold-out cross-validation (CV) indicated good model performance (10-fold CV-R$^2$, 0.86 and 0.85 for PM$_{2.5}$ in 2000 and 2010, respectively) and (0.60 and 0.57 for PM$_{10}$). Further detail on PM$_{2.5}$ and PM$_{10}$ modeling is provided elsewhere (Kim et al., in prep). Annual PM$_{2.5}$ and PM$_{10}$ concentrations were also predicted at populated 2000 and 2010 census block centroids. Average concentrations for PM$_{2.5}$ and PM$_{10}$ between 2000 and 2010 in populated census blocks dropped from 12.1 μg/m$^3$ to 9.0 μg/m$^3$ for PM$_{2.5}$ and 21.5 μg/m$^3$ to 17.9 μg/m$^3$ for PM$_{10}$ (Table 2). Since census blocks changed between census years (2000 vs 2010) predictions for PM$_{2.5}$ and PM$_{10}$ for the year 2000 were made using NHGIS crosswalks, which are missing 230,904 blocks (representing 538,762 children, or <1% of the total). The impact of these <1% of missing data is unlikely large.

2.5. Concentration-response function

We obtained concentration-response functions (CRF) for the association between exposure to the three pollutants and the subsequent development of childhood asthma from a meta-analysis published by Khreis et al. (2017). The meta-analyses synthesized a total of 41 studies that examined the association between children’s exposure to TRAP metrics and their risk of subsequent asthma, incidence or lifetime prevalence, from birth to 18 years old. Random-effects meta-analyses were selected to summarize the risk estimates across the range of studies, as they account for within study variance caused by chance and sampling error, but also for between studies variance caused by heterogeneity (Kirkwood and Sterne, 2003), a feature that is likely to be present in studies of TRAP and asthma development (Health Effects Institute, 2010).

The CRF for NO$_2$ was 1.05 (95% CI = 1.02–1.07) per 4 μg/m$^3$, for PM$_{2.5}$, it was 1.03 (95% CI = 1.01–1.05) per 1 μg/m$^3$, and for PM$_{10}$, it was 1.05 (95% CI = 1.02–1.08) per 2 μg/m$^3$. The NO$_2$ CRF was based on 20 studies, while PM$_{2.5}$ and PM$_{10}$ CRF were based on 10 and 12 studies, respectively. It is worth noting here that the studies included in the underlying meta-analyses did not adjust for co-pollutants. As such, the numbers of asthma cases attributable to NO$_2$, PM$_{2.5}$ and PM$_{10}$ should not simply be added. Instead, these estimates should be viewed as independent estimates of the potential impact of different traffic related air pollutants.

2.6. Burden of disease model

Combining children population counts, asthma incidence rate, pollutant-specific CRF and pollutant concentrations, we estimated the total number of new incident asthma cases attributable to exposure to each pollutant and in each year, separately. We used standard burden of disease assessment methods (Mueller et al., 2017), following the steps below:

First, we estimated the number of new asthma cases for that year (asthma incident cases) by multiplying the number of at-risk children in that year by the incidence rate.

\[ At = \text{risk children} \times \text{Total children} \times \text{Prevalence rate} \]  \hspace{1cm} (1)

\[ \text{Asthma incident cases} = \text{At} - \text{risk children} \times \text{Incidence rate} \]  \hspace{1cm} (2)

Second, we estimated the relative risk (RR$_{diff}$) associated with the exposure difference between the current exposure and the counterfactual exposure (zero air pollution) scenarios.

\[ \text{RR}_{diff} = e^{(\ln(\text{RR})/\text{RRunit}) \times \text{Exposure level}} \]  \hspace{1cm} (3)

where RR is the relative risk obtained from the CRF.

\[ \text{RRunit} = \text{the exposure unit of the RR obtained from the CRF}. \]

Third, using the RR$_{diff}$, we estimated the percentage of asthma incident cases due to each pollutant’s exposure, otherwise known as the population attributable fraction (PAF).

\[ \text{PAF} = (\text{RR}_{diff} - 1)/(\text{RR}_{diff}) \]  \hspace{1cm} (4)

Using the PAF, we estimated the number of asthma incidence cases due to each pollutant’s exposure known as the attributable number of cases (AC).

\[ \text{AC} = \text{PAF} \times \text{Asthma incident cases} \]  \hspace{1cm} (5)

Finally, we summed up the AC across all the included census blocks, separately for each pollutant and each year.

2.7. Counterfactual scenarios

In the counterfactual scenarios, we assumed that TRAP did not exceed a certain annual average limit at any census block for each pollutant and year separately using two scenarios:

1. TRAP levels did not exceed the World Health Organization (WHO) air quality guideline values as shown below:
   a. NO$_2$ was 40 μg/m$^3$ (annual average);
   b. PM$_{2.5}$ was 10 μg/m$^3$ (annual average);
   c. PM$_{10}$ was 20 μg/m$^3$ (annual average).

2. TRAP levels did not exceed the minimum modeled concentration by the LUR models at any census block in either year as shown below:
   a. NO$_2$ was 1.48 μg/m$^3$ (annual average);
   b. PM$_{2.5}$ was 0.55 μg/m$^3$ (annual average);
   c. PM$_{10}$ was 0.72 μg/m$^3$ (annual average).

We then reran our analysis, following the steps outlined in Section 2.6, and estimated the number of incident asthma cases due to TRAP which could have been prevented among census blocks that exceeded annual average limits for the two scenarios.

2.8. Sensitivity analyses

In our sensitivity analysis, we examined the range of uncertainty in the burden of disease estimates. For this purpose, we re-ran our analysis using all possible combinations of the upper and lower 95% CI of both the CRF and the asthma incidence rate. We produced a sensitivity analysis matrix summarizing all possible combinations of 95% CI bounds for the CRF and incidence rate.

2.9. Joining of data and running the analysis

We joined all data sets using a unique identifier for each census block and the pollutant estimates. Each census block contained information on the population count, urban or rural category, median household income group and pollutant estimates at the centroid coordinate of the block. For all analysis we used the software R version 3.4.3 (2017-11-30). We produce open-access interactive maps summarizing the data at the county level using the leaflet package in R (Joe et al., 2018; R Core Team, 2018). We also produce a look up table summarizing the data at the city level for 498 major cities in the US which were selected from the CDC’s 500 cities project, as described in detail at [https://www.cdc.gov/500cities/index.htm]. Two cities: Anchorage, Alaska and Honolulu, Hawaii were excluded from the 500
cities list, as we lacked exposure data for these states. Both the interactive maps and the look up table are available at [https://cartehdata.org/l/s/TRAP-burden-of-childhood-asthma](https://cartehdata.org/l/s/TRAP-burden-of-childhood-asthma).

3. Main results

3.1. Overall asthma incident cases

Based on the available childhood asthma incidence rate, the estimated total number of incident cases was 786,290 and 794,934 in 2000 and 2010, respectively (see Table 3). As shown in Tables 1, 79% and 81% of the total child population (and therefore the estimated incident cases) were living in an urban area in 2000 and 2010. The largest percentage of total incident cases (31%) lived in census block groups with a median household income of $35,000 to <$50,000 in 2000 and (30%) lived in a census block groups with a median household income of $50,000 to <$75,000 in 2010 (Table 3).

3.2. Attributable number of asthma incident cases

Rounded to the nearest hundred, we estimated on average 209,100 and 141,900 attributable cases due to NO$_2$ in 2000 and 2010, respectively, which accounted for 27% and 18% of all childhood asthma incident cases (see Table 3). As shown in Tables 1, 79% and 81% of the total child population (and therefore the estimated incident cases) were living in an urban area in 2000 and 2010. The largest percentage of total incident cases (31%) lived in census block groups with a median household income of $35,000 to <$50,000 in 2000 and (30%) lived in a census block groups with a median household income of $50,000 to <$75,000 in 2010 (Table 3).

3.3. Attributable number of asthma incident cases by living location

Most attributable cases clustered in urban areas (see Table 4 and Figs. S5–S6), and this was particularly prominent in the NO$_2$ analysis. 184,500 and 127,500 of cases attributable to NO$_2$ lived in an urban area in 2000 and 2010, with 30% and 20% of cases were due to NO$_2$. While in rural areas, only 15% and 10% of cases were due to NO$_2$ in 2000 and 2010, respectively. For PM$_{2.5}$, the attributable number of cases living in an urban area were 200,100 and 190,200 for 2000 and 2010, respectively, which accounted for 31% and 24% of all childhood asthma incident cases. Cases due to PM$_{10}$ were estimated to be 331,200 and 286,500 in 2000 and 2010, respectively, which accounted for the highest percentage of overall childhood asthma incident cases at 42% and 36%.

4. Preventable cases of counterfactual scenarios

Table 5 presents a summary of the preventable number of cases in the two counterfactual scenarios.

4.1. Preventable number of asthma incident cases if blocks hadn’t exceeded WHO air quality guideline values

The estimated preventable number of asthma incident cases had census blocks not exceeded the WHO air quality guideline values were as follows:

- For NO$_2$, with an annual average concentration of 40 μg/m$^3$ as a limit, there was an estimated 11,100 (1% of all asthma cases) and 300 (<1%) preventable asthma incident cases in 2000 and 2010, respectively.
- For PM$_{2.5}$, with an annual average concentration of 10 μg/m$^3$ as a limit, there was an estimated 53,400 (7%) and 9500 (1%) preventable asthma incident cases in 2000 and 2010, respectively.
- For PM$_{10}$, with an annual average concentration of 20 μg/m$^3$ as a limit, there was an estimated 43,900 (6%) and 14,400 (2%) preventable asthma incident cases in 2000 and 2010, respectively.

4.2. Preventable number of asthma incident cases if pollutant concentrations were reduced to minimum levels

The estimated preventable number of asthma incident cases had pollutant concentrations for all census blocks reduced to the minimum levels modeled were as following:

- For NO$_2$, with a minimum level of 1.48 μg/m$^3$ as a limit, there was an estimated 188,300 (24% of all asthma cases) and 127,700 (16%) preventable asthma incident cases in 2000 and 2010, respectively.
- For PM$_{2.5}$, with a minimum level of 0.55 μg/m$^3$ as a limit, there was an estimated 234,500 (30%) and 177,400 (22%) preventable asthma incident cases in 2000 and 2010, respectively.
- For PM$_{10}$, with a minimum level of 0.72 μg/m$^3$ as a limit, there was an estimated 317,700 (40%) and 272,700 (34%) preventable asthma incident cases in 2000 and 2010, respectively.

5. Results of sensitivity analyses

To produce the most conservative and most extreme estimates, and explore the impact of uncertainty in the CRF, the incidence rate used, and the combination thereof on the estimated burden of disease, we ran multiple sensitivity analyses and report them in Tables 6, S3 and S4.

5.1. Most conservative estimates

For the most conservative estimates, the analysis was repeated using the lower 95% CI bound for both the CRF and the incidence rate. The

<table>
<thead>
<tr>
<th>Table 3 Estimated asthma incident cases among children.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estimated asthma incident cases among children</td>
</tr>
<tr>
<td>Asthma incident cases</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>By living location (% of Total)</td>
</tr>
<tr>
<td>Urban</td>
</tr>
<tr>
<td>Rural</td>
</tr>
<tr>
<td>By median household income</td>
</tr>
<tr>
<td>&lt;20,000</td>
</tr>
<tr>
<td>20,000 to &lt;35,000</td>
</tr>
<tr>
<td>35,000 to &lt;50,000</td>
</tr>
<tr>
<td>50,000 to &lt;75,000</td>
</tr>
<tr>
<td>≥75,000</td>
</tr>
</tbody>
</table>

* Not applicable, we could not adjust for inflation.
Table 4
Attributable number of childhood asthma incident cases and percentage of asthma incident cases due to TRAP.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>AC 2000</th>
<th>% of all asthma cases 2000</th>
<th>Change (%) 2000-2010</th>
<th>AC 2010</th>
<th>% of all asthma cases 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO2 Total</td>
<td>209,100</td>
<td>141,900</td>
<td>27%</td>
<td>18%</td>
<td>32%</td>
</tr>
<tr>
<td>By living</td>
<td>Urban 184,500</td>
<td>127,500</td>
<td>30%</td>
<td>20%</td>
<td>31%</td>
</tr>
<tr>
<td>By median household income</td>
<td>&lt;20,000 20,000-25,000</td>
<td>99,600 25,000-30,000</td>
<td>64%</td>
<td>35%</td>
<td>11%</td>
</tr>
<tr>
<td>PM2.5 Total</td>
<td>247,100</td>
<td>190,200</td>
<td>31%</td>
<td>24%</td>
<td>32%</td>
</tr>
<tr>
<td>By living</td>
<td>Urban 200,100</td>
<td>158,200</td>
<td>32%</td>
<td>24%</td>
<td>21%</td>
</tr>
<tr>
<td>By median household income</td>
<td>&lt;20,000 20,000-35,000</td>
<td>74,900 35,000-50,000</td>
<td>73%</td>
<td>23%</td>
<td>N/A</td>
</tr>
<tr>
<td>PM10 Total</td>
<td>331,200</td>
<td>286,500</td>
<td>42%</td>
<td>36%</td>
<td>13%</td>
</tr>
<tr>
<td>By living</td>
<td>Urban 270,100</td>
<td>240,600</td>
<td>44%</td>
<td>37%</td>
<td>11%</td>
</tr>
<tr>
<td>By median household income</td>
<td>&lt;20,000 20,000-100,000</td>
<td>98,300 100,000-200,000</td>
<td>39%</td>
<td>13%</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Sensitivity analysis of attributable number of cases.

Table 6
Sensitivity analysis of attributable number of cases.

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Concentration response function</th>
<th>Mean AC</th>
<th>% of all asthma cases</th>
<th>Mean AF</th>
<th>% of all asthma cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO2</td>
<td>CRF</td>
<td>227,200</td>
<td>35%</td>
<td>35%</td>
<td>36%</td>
</tr>
<tr>
<td>PM2.5</td>
<td>CRF</td>
<td>141,900</td>
<td>34%</td>
<td>36%</td>
<td>37%</td>
</tr>
<tr>
<td>PM10</td>
<td>INCidence rate</td>
<td>158,800</td>
<td>35%</td>
<td>36%</td>
<td>37%</td>
</tr>
</tbody>
</table>

Estimates using mean concentration-response function and mean incidence rate, as shown in (Table 4).

6. Discussion

6.1. Summary and key findings

Our study is the first to examine TRAP exposures and the burden of childhood asthma development in the US on a national scale, using exposure levels at the smallest available geographical unit and meta-analysis derived CRF. Our findings, based on emerging evidence that TRAP leads to the onset of asthma among children, suggest that TRAP is responsible for the development of a large portion of preventable childhood asthma in the US.

Between 141,900 (18%) and 331,200 (42%) of childhood asthma was attributable to TRAP. The burden of disease varied depending on the pollutant that was selected in the analysis; our results suggest that NO2 contributes to the least burden of disease while PM10 contributes to the most. However, it is important to note that traffic contributes different pollutants to urban air pollution at varying degrees, for example, studies in Europe have demonstrated that traffic contributes to over 80% of NO2 (between 9 and 66% of PM2.5 and 9–53% of PM10 (Sundvor et al., 2012). Hence, NO2, which is a more specific surrogate of the TRAP mixture when compared to particulate matter, may better represent the burden associated with traffic emissions in particular (Beckerman et al., 2008; Karner et al., 2010; Zhou and Levy, 2007).

Over the 10-year period of our analysis, the attributable number of incident asthma cases due to all the pollutants decreased. Reduction in NO2 levels was the most prominent among pollutants and accounted for a 33% reduction in the estimated burden of disease. This is mainly due to a reduction in estimated air pollution concentrations (Clark et al., 2017), as the asthma incidence rate we used in our analysis remained unchanged and the total number of incident cases among children only increased by 1% during the same time period.

Moreover, we found that children living in urban areas had twice the percentage of asthma cases attributable to NO2 exposures as compared to children living in rural areas (30% versus 15% in 2000 and 20% versus 10% in 2010). This is due to the higher average levels of NO2 in urban areas as compared to rural areas, as shown in Table S2. This contrast was not as great for PM2.5, which had only a 4% and 2% absolute difference in percent of asthma incident cases between urban and rural locations, while PM10 had an absolute difference of 8% and 6% in 2000 and 2010, respectively. Finally, children living in census block groups with a lower median household income had slightly lower 95% CI of both the CRF and incidence rate.

attributable number of asthma incidence cases due to TRAP reduced by 60%–69% (Table 6, Table S3 and Table S4).

5.2. Most extreme estimates

For the most extreme estimates the analysis was repeated using the upper 95% CI of both the CRF and incidence rate. The attributable number of asthma incidence cases due to TRAP increased by 49%–74% (Table 6, Table S3 and Table S4).
higher percentage of attributable incident cases than children living in areas with a higher median income. Our results are in line with previously published data showing that, on average, households with lower income were more likely to live near high density traffic (Clark et al., 2017; Rowangould, 2013). The only exception was in NO2 exposure in 2000, in which, the highest median household income group had the second largest percentage of attributable cases.

6.2. Comparison with previous studies

A few studies estimating the burden of asthma due to TRAP were previously published. In a study of 10 European cities, the burden of asthma attributable to TRAP had an average of 14% and ranged from 7% to 23% (Perez et al., 2013). Another study in Los Angeles, California reported a range between 6% and 9% (Perez et al., 2009). Both estimates were lower than our range of 18% to 42%. However, both of the above studies used a proximity to major roadways measure as a surrogate of TRAP exposures where children living within a 75 m buffer of main roadways were classified as exposed. In the Los Angeles study by Perez et al. (2009), only 20% of the total children’s population lived near a main roadway while in Europe this percentage was higher at 31% with a range of 14% to 56%, depending on the city (Perez et al., 2013). In our study, all kids were exposed (albeit to different levels of air pollution), and as such both studies using the proximity measure might have resulted in a large portion of the population being misclassified as non-exposed. A study by Ryan et al. (2007) examining associations between infant wheezing and residing within 100 m from stop-and-go bus and truck traffic showed that using a LUR model may reduce exposure misclassification that arises from a proximity model. A more recent study by Khreis et al. (2018a) using a LUR model, estimated that 24% of all new childhood asthma in the city of Bradford, United Kingdom, were attributable to NO2. In their follow-up study, Khreis et al. (2018b) reported that the PM2.5, PM10, and Black Carbon exposures accounted for 15% to 33% of all new childhood asthma cases in Bradford. Our results are therefore comparable to estimates reported in the English studies despite being higher.

6.3. Strengths and limitations

We used meta-analysis derived CRF of continuous pollutant exposures (Khreis et al., 2017), as opposed to a single CRF using a proximity measure (McConnell et al., 2006). Using a meta-analysis derived CRF would be more appropriate when extrapolating to a national scale and different locations. A meta-analysis derived CRF would also overcome statistical uncertainty associated from a single study and would better address heterogeneity among different populations. Further, our CRF were pollutant-specific and are better suited to capture the impact of the spatial variability of the different air pollutants. Although most studies included in the meta-analysis adjusted for major confounders (e.g. socioeconomic status, smoking, parental atopy) (Khreis et al., 2017), there were no specific CRFs based on these variables (e.g. a CRF for low versus high median household income), and as such we could not account for this in our analysis. However, we stratified the results by living location and median household income to simply visualize the burden of disease, without using different CRFs and incidence rates across these strata, as this information is predominantly lacking in the literature. Although this is a simplification of the analysis, it is still useful to show these stratified estimates and this approach is in line with wider literature cited above.

In our study, we used a childhood asthma incidence rate instead of a prevalence rate. The main advantage of doing so is that we were able to estimate the number of preventable cases of childhood asthma; had there been reduced exposures to the pollutants we investigated. However, the incidence rate itself had some noteworthy limitations. First, the ACBS aggregated the rates for the years 2006 through 2008 which do not cover the time period of our study (2000 and 2010). Second, not all states participated in the survey for each year (Winer et al., 2012), hence the incidence rate is not representative of all states. Although these limitations might result in different incidence rates, and therefore different burden of disease estimates, we believe that our results are robust due to two points. First, we do not believe that the incidence rate would vary significantly during a relatively short period of time. For example, asthma prevalence for children was 8.7% in 2001 and increased to only 9.7% in 2010 (Moorman et al., 2012). Second, our sensitivity analysis showed that changing the incidence rate to the lower (10.5 per 1000 child per year) and upper (14.4 per 1000 child per year) CI bounds would change the mean estimate of attributable number of cases for all pollutants by no >16% (Table S3). Another limitation is that Winer et al. (2012) used self-reported doctor diagnosis to identify an asthma case. This approach will likely lead to an overestimation of the number of cases in our analysis. However, studies/data sets estimating asthma incidence using more specific objective methods, and at local scales, are not available. When future data becomes available, our models can be reconfigured to more accurately estimate the number of attributable asthma cases.

Although the LUR predicts air pollution with fairly high accuracy, it considers all sources of air pollution and we could not parcel out the exact contribution of traffic from other sources in the exposure and associated burden of disease. For example, the 2014 National Emissions Inventory Report describes four major sources of air pollution emissions: stationary sources (e.g. fuel combustion for electricity generation, industrial process like fertilizer application), fires, biogenics (naturally occurring emissions) and mobile sources. Mobile sources include on-road (traffic) and non-road sources (e.g. aircrafts and marine sources). The report estimated that between 2002 and 2011 around 41% of Nitrogen Oxides emissions were from on-road sources, 21% from non-road sources, 37% from stationary sources (e.g. fuel combustion) and the remaining from other sources. For PM10, stationary sources accounted for 90% of emissions and <2% were from on-road sources, while for PM2.5, stationary sources accounted for 70% of emissions and <5% of emissions were from on-road sources (EPA, 2014). It is important to note that these ratios are generic from across the whole of the US: both urban and rural emissions combined. For NO2 and PM2.5, we posit that the proportion of total concentrations that are attributable to traffic is higher in urban areas than in rural areas. Our approach, therefore, would lead to an overestimation of the burden of asthma “due to TRAP”; this overestimation would be greater in rural areas than in urban areas. Most of the child population in this analysis lived in an urban setting (~80%).

It is also important to note that the Census Bureau categorizes urban areas using several criteria including population threshold, density, land use and distance. Urban areas are subdivided into two types, urbanized areas with a population of 50,000 or more and urban clusters with at least 2500 but fewer than 50,000 people. In order for a census block to be defined as urban it must have a population density of at least 1000 people per square mile (ppsm), or 500 ppsm if the block contains a mix of residential and nonresidential land use (e.g. parks, retail, schools), or contains nonresidential land use with a high amount of impervious surface while distanced within a quarter mile of an urban area. Rural is defined as all population, housing, and territory not included within an urbanized area or urban cluster. TRAP exposure surrogates more correctly relate to an urban setting with high levels of people and traffic, since the level of pollution from traffic sources as a ratio of ambient pollution is higher in urban settings compared to rural settings. Therefore, the use of pollutant surrogates (NO2, PM2.5 and PM10) as a measure for TRAP would overestimate TRAP exposures and the attributable cases, more in rural areas than in urban areas. The LUR models also estimated concentrations at the centroid of census blocks, which could be a farther point from roadways since census blocks are usually delineated by roadways (US Census Bureau, 1994). However, we could not verify how this would affect the direction of exposure since calculating the average concentration at a finer scale within...
census blocks wasn’t feasible in this project, due to the large computational intensity needed to predict values across the contiguous US. We also assigned exposures at the residential location while variability in exposure at the indoor, outdoor and personal levels were not considered. This is in line with the meta-analysis derived CRF we used, which were predominantly based on residential locations (Khreis et al., 2017). However, previous research suggests that personal exposure to pollutants is usually higher than indoor and outdoor concentrations which might result in underestimating exposure levels and the associated burden of disease (Monn, 2001). Finally, our analysis assumes TRAP is causally associated with the development of childhood asthma. However, there remains some level of uncertainty. First, the studies included in the underlying meta-analysis had different levels of heterogeneity. For example, Khreis et al. (2017) showed that the largest heterogeneity among the pollutants was with NO₂, suggesting that NO₂ may act as a surrogate for another pollutant(s) in the mixture. Possible interactions between pollutants was not considered; and it is uncertain whether pollutants act in single or multiple causal pathways leading to the development of asthma. Second, it is uncertain if there are other confounders that would still cause asthma cases even if the TRAP exposure was eliminated, which may lead to an overestimation of the burden attributable to TRAP. Third, Khreis et al. (2017) indicated that the most common method of identifying asthma between studies underlying the meta-analysis was by using parental-reporting of doctor-diagnosis. Although this method is in line with how we estimated the national childhood asthma incidence rate, it may lead to classification errors, especially among younger children in which symptoms of respiratory illnesses overlap (Castro-Rodríguez et al., 2006; Werk et al., 2000).

### 6.4. Summary and conclusions

Our study contributes to the scarce literature estimating the burden of childhood asthma attributable to TRAP and the first in estimating on a national scale for the US, while also presenting the results for the major 498 US cities. We utilized the best available datasets; using small scale geographical units for both the census data and pollutant concentrations and meta-analysis derived CRF which enabled us to estimate the burden attributable to NO₂, PM₂.₅ and PM₁₀ separately. On average, the estimated percentage of childhood asthma incident cases attributable to TRAP in the contiguous US ranged between 18% and 42%, depending on the year and pollutant selected in the analysis. The reduction in air pollution concentrations over the 10-year study period translated in a drop of up to 33% in the number and percentage of attributable childhood asthma cases due to TRAP. However, our results indicate that these pollutants are still responsible for a large portion of preventable childhood asthma cases: up to 286,500 cases in 2010. For PM₂.₅ and PM₁₀, our results are likely to be an overestimate of the impact of traffic sources on childhood asthma, mainly because the LUR model predictions aim to reflect all sources of air pollution, which are significant for PM. Due to the scarcity of recent asthma incidence studies, we were unable to take into account the varying spatial distribution of childhood asthma incidence, for example at urban versus rural locations. Future studies which measure childhood asthma incidence rates at a finer scale and can parse out the exact traffic contribution to overall air pollution exposures are needed to improve the burden of disease assessment due to TRAP. Overall, we estimate that reducing pollutant levels in the US from 2010 levels to levels that are compliant with the WHO air quality guidelines would reduce new childhood asthma cases by up to 14,400 cases (2% of all asthma cases) and a further reduction to the lowest modeled levels would reduce new childhood asthma cases by up to 272,700 cases (34% of all asthma cases).

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### Competing financial interests

The authors declare they have no competing interests.

### Appendix A. Supplementary data

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### References


