Environment International xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

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

Raed Alotaibi[a,b,c], Mathew Bechle[d], Julian D. Marshall[d], Tara Ramani[a], Josias Zietsman[a], Mark J. Nieuwenhuijsen[e,f,g], Haneen Khreis[a,e,f,g,*]

[a] Center for Advancing Research in Transportation Emissions, Energy, and Health (CARTEEH), Texas A&M Transportation Institute (TTI), TX, USA
[b] Department of Family and Community Medicine, Imam Abdulrahman Bin Faisal University, Saudi Arabia
[c] Texas A&M Health Science Center School of Public Health, TX, USA
[d] Department of Civil and Environmental Engineering, University of Washington, Seattle, WA, USA
[e] ISGlobal, Centre for Research in Environmental Epidemiology (CREAL), Barcelona, Spain
[f] Universitat Pompeu Fabra (UPF), Barcelona, Spain
[g] CIBER Epidemiologia y Salud Publica (CIBERESP), Madrid, Spain

ARTICLE INFO

Handling Editor: Xavier Querol

Keywords:
Traffic related air pollution
Burden of disease
Asthma
Children
United States

ABSTRACT

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). NO_2, $PM_{2.5}$ and PM_{10} were used as *surrogates* of TRAP exposures, with NO_2 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/m^3 for NO_2, 12.1 and 9 μg/m^3 for $PM_{2.5}$ and 21.5 and 17.9 μg/m^3 for PM_{10}. 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, 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 a

Abbreviations: AC, attributable number of cases; ACBS, Asthma Call Back Survey; BRFSS, Behavioral Risk Factor Surveillance System; CDC, Centers for Disease Control and Prevention; CRF, concentration response function; EPA, Environmental Protection Agency; LUR, land-use regression; NHGIS, National Historical Geographic Information System; NO_2, nitrogen dioxide; O_3, ozone; PAF, population attributable fraction; PM_{10}, particulate matter 10 μm or less in diameter; $PM_{2.5}$, particulate matter 2.5 μm or less in diameter; TRAP, traffic related air pollution; US, United States of America; WHO, World Health Organization

* Corresponding author at: Center for Advancing Research in Transportation Emissions, Energy, and Health (CARTEEH), Texas A&M Transportation Institute (TTI), 2929 Research Parkway, 3135 TAMU, College Station, TX 77843-3135, USA.
E-mail address: H-Khreis@tti.tamu.edu (H. Khreis).

https://doi.org/10.1016/j.envint.2019.03.041
Received 27 October 2018; Received in revised form 8 February 2019; Accepted 16 March 2019

national scale in the US. The attributable burden of childhood asthma dropped by 33% between 2000 and 2010. However, a significant proportion of cases can be prevented.

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 subphenotypes. 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 (Krzyzanowski 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 NO_2, elemental carbon (EC) or Black Carbon (BC), PM, benzene, and ultrafine particles (UFP) (Health Effects Institute, 2010). NO_2 and BC are considered better traffic surrogates compared to $PM_{2.5}$ and PM_{10} 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 NO_2, but not $PM_{2.5}$, 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, NO_2, $PM_{2.5}$ and PM_{10} 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 NO_2 and $PM_{2.5}$ 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 NO_2 and 1.25 (95% CI = 1.06–1.46) for $PM_{2.5}$ (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., 2013). 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 NO_2 and Ozone (O_3) 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 NO_2, $PM_{2.5}$ and PM_{10} concentrations as surrogates of the TRAP mixture across all populated US census blocks for years 2000 and 2010. NO_2 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 $\mu g/m^3$ for NO_2, $PM_{2.5}$ and PM_{10} for the years 2000 and 2010 at the centroid of all included census blocks. NO_2 concentrations were converted from ppb to $\mu g/m^3$ 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. NO_2 models

The NO_2 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 NO_2 concentrations alongside several covariates (for example, impervious surfaces, elevation, major roads, residential roads, and distance to coast) to estimate

Table 1
Census data description.

Census data description			
	2000	2010	Change (%)
Geographic characteristics			
Total populated census blocks	5,280,214	6,182,882	17%
Total census-designated urban Areas	2,970,347 (56%)	3,590,278 (58%)	21%
Demographic characteristics			
Total population	279,583,437	306,675,006	10%
Total population of children (birth - 18)	71,807,328 (26%)	73,690,271 (24%)	3%
Mean (range) number of children in census blocks	14 (0–4713)	12 (0–2214)	−12%
Population of children by living location			
Urban	56,504,832 (79%)	59,927,088 (81%)	6%
Rural	15,302,496 (21%)	13,763,183 (19%)	−10%
Population of children by median household income			
< 20,000	4,055,407 (6%)	2,614,804 (4%)	N/A[a]
20,000 to < 35,000	20,694,588 (29%)	12,770,843 (17%)	
35,000 to < 50,000	21,974,042 (31%)	18,573,954 (25%)	
50,000 to < 75,000	17,350,990 (24%)	21,953,876 (30%)	
≥ 75,000	7,732,301 (11%)	17,763,239 (24%)	

[a] Not applicable, we could not adjust for inflation.

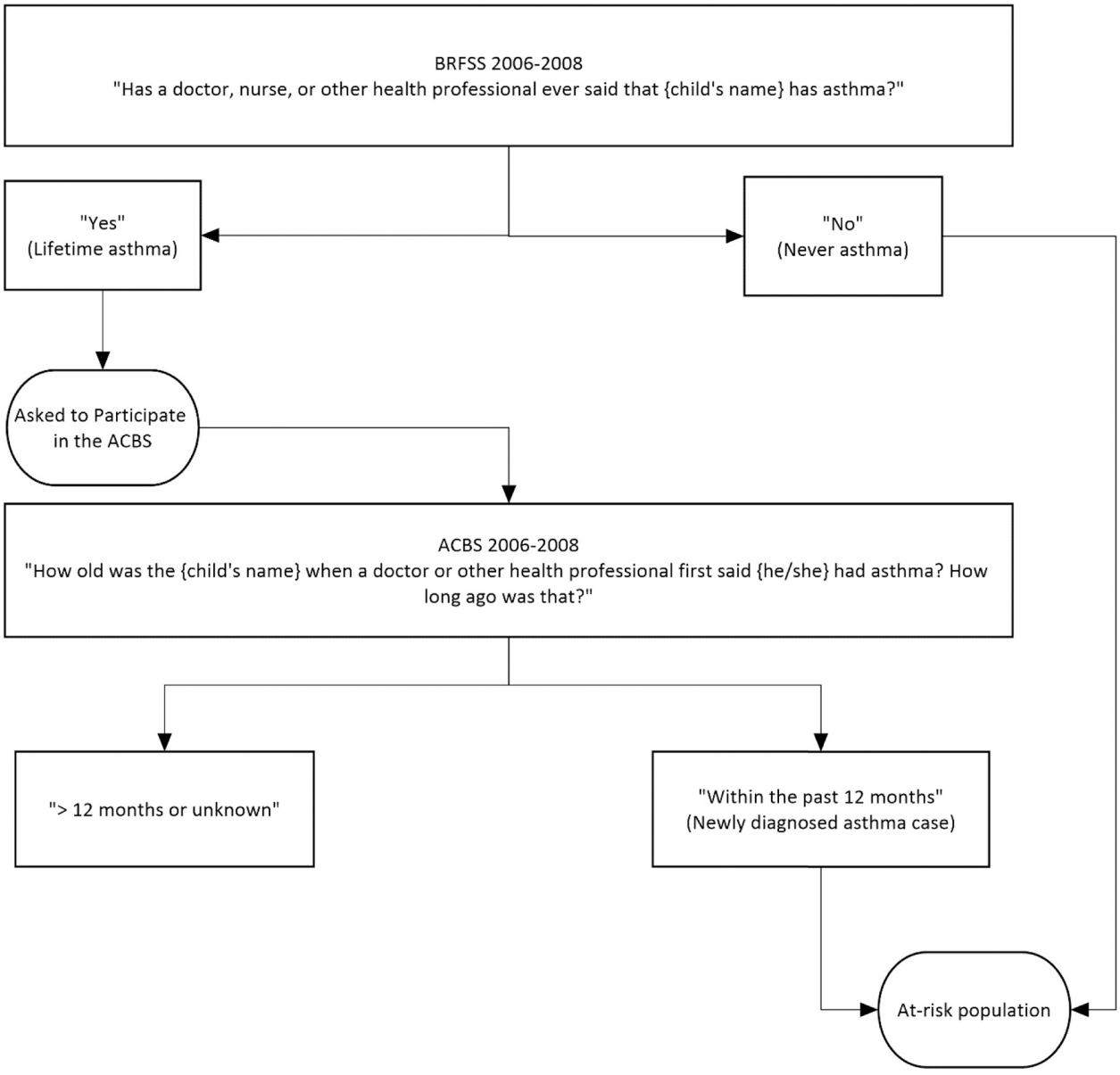

Fig. 1. "Never asthma", "Newly diagnosed asthma case" and "At-risk population" from the Behavioral Risk Factor Surveillance System (BRFSS) and Asthma Call-back Survey (ACBS) data sets, 2006–2008.

NO_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 ($R^2 = 0.82$); which is comparable with other continental-scale NO_2 LUR models (Beelen et al., 2009; Hystad et al., 2011; Novotny et al., 2011; Vienneau et al., 2013). The population-weighted average NO_2 concentration in the US decreased from 20.6 μg/m^3 in 2000 to 13.2 μg/m^3 in 2010 (Table 2).

Table 2
Summary of pollutant concentrations using populated census blocks only.

Population-weighted average concentrations									
Pollutant	NO_2 μg/m^3			$PM_{2.5}$ μg/m^3			PM_{10} μg/m^3		
	2000	2010	Change (%)	2000	2010	Change (%)	2000	2010	Change (%)
Mean	20.6	13.2	−36%	12.1	9.0	−26%	21.5	17.9	−17%
Min	2.2	1.5	−32%	0.6	1.3	117%	2.8	0.7	−75%
25%	12.1	7.9	−35%	9.8	7.4	−24%	18	14.6	−19%
50%	17.9	11.4	−36%	12.2	9.1	−25%	21.3	17.8	−16%
75%	26.3	16.6	−37%	14.5	10.6	−27%	24.2	21.2	−12%
Max	95.9	58.3	−39%	26.4	16.6	−37%	73.7	49.1	−33%

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.

$$At-risk\ children = Total\ children - (Total\ children * Prevalence\ rate) \quad (1)$$

$$Asthma\ incident\ cases = At-risk\ children * Incidence\ rate \quad (2)$$

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.

$$RR_{diff} = e^{((\ln(RR)/RRunit)*\text{Exposure level})} \quad (3)$$

where RR is the relative risk obtained from the CRF.

RR_{unit} is 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).

$$PAF = (RR_{diff} - 1)/(RR_{diff}) \quad (4)$$

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

$$AC = PAF*\text{Asthma incident cases} \quad (5)$$

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://carteehdata.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 4 and Figs. S3–S5). For $PM_{2.5}$, the number of attributable cases was 247,100 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%.

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 158,200, with 32% and 24% of cases were due to $PM_{2.5}$ in 2000 and 2010, respectively. While in rural areas, only 28% and 22% of cases were due to $PM_{2.5}$, in 2000 and 2010. For PM_{10}, the attributable number of cases living in an urban area were 270,100 and 240,800, with 44% and 37% of cases were due to PM_{10} in 2000 and 2010, respectively. While in rural areas, only 36% and 31% of cases were due to PM_{10}, in 2000 and 2010.

3.4. Attributable number of asthma incident cases by median household income

The most deprived median household income group (<$20,000) had the highest percentage of asthma cases due to NO_2 among all cases at 31% and 21% for 2000 and 2010, respectively. The second highest percentage of asthma incident cases due to NO_2 was among the highest income group (≥$75,000) for year 2000 at 29% of all cases. However, for 2010 the second highest percentage of asthma incident cases due to NO_2 was for the median household income group of $20,000 to <$35,000; the second lowest. For $PM_{2.5}$, the highest percentage of asthma incident cases was among the lowest median household income group for both years at 33% and 26%. For PM_{10}, the highest percentage of asthma incident cases was also among the lowest median household income group for both years at 45% and 38% (Table 4 and Figs. S7–S8).

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 reran 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 3
Estimated asthma incident cases among children.

Estimated asthma incident cases among children			
Asthma incident cases	2000	2010	Change (%)
Total	786,290	794,934	1.1%
By living location (% of Total)			
Urban	618,728 (79%)	646,463 (81%)	4%
Rural	167,562 (21%)	148,470 (19%)	−11%
By median household income			
<20,000	44,407 (6%)	28,207 (4%)	N/A[a]
20,000 to <35,000	226,606 (29%)	137,765 (17%)	
35,000 to <50,000	240,616 (31%)	200,367 (25%)	
50,000 to <75,000	189,993 (24%)	236,827 (30%)	
≥75,000	84,669 (11%)	191,621 (24%)	

[a] 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.

Attributable number of cases and percentage of all cases							
		AC		% of all asthma cases		Change (%)	
		2000	2010	2000	2010	AC	AF
NO_2							
Total		209,100	141,900	27%	18%	−32%	−33%
By living location	Urban	184,500	127,500	30%	20%	−31%	−33%
	Rural	24,600	14,500	15%	10%	−41%	−33%
By median household income	<20,000	13,700	5900	31%	21%	N/A[a]	N/A[a]
	20,000 to <35,000	59,600	25,800	26%	19%		
	35,000 to <50,000	60,700	34,600	25%	17%		
	50,000 to <75,000	50,900	40,500	27%	17%		
	≥ 75,000	24,100	35,100	29%	18%		
$PM_{2.5}$							
Total		247,100	190,200	31%	24%	−23%	−24%
By living location	Urban	200,100	158,200	32%	24%	−21%	−24%
	Rural	47,100	32,000	28%	22%	−32%	−23%
By median household income	<20,000	14,600	7400	33%	26%	N/A[a]	N/A[a]
	20,000 to <35,000	71,600	34,600	32%	25%		
	35,000 to <50,000	74,900	48,300	31%	24%		
	50,000 to <75,000	59,400	55,700	31%	24%		
	≥75,000	26,700	44,100	32%	23%		
PM_{10}							
Total		331,200	286,500	42%	36%	−13%	−14%
By living location	Urban	270,100	240,800	44%	37%	−11%	−16%
	Rural	61,100	45,700	36%	31%	−25%	−14%
By median household income	<20,000	19,800	10,700	45%	38%	N/A[a]	N/A[a]
	20,000 to <35,000	98,300	51,300	43%	37%		
	35,000 to <50,000	100,800	72,300	42%	36%		
	50,000 to <75,000	78,700	85,000	41%	36%		
	≥75,000	33,700	67,300	40%	35%		

Numbers rounded to nearest hundred.
[a] Not applicable, we could not adjust for inflation.

Table 5
Preventable number of asthma incident cases exceeding the "safe levels".

Preventable number of asthma incident cases exceeding the "safe levels"				
	2000		2010	
	AC	% of all asthma cases	AC	% of all asthma cases
WHO guidelines "safe level"				
NO_2	11,100	1%	300	<1%
$PM_{2.5}$	53,400	7%	9500	1%
PM_{10}	43,900	6%	14,400	2%
Minimum concentration "safe level"				
NO_2	188,300	24%	127,700	16%
$PM_{2.5}$	234,500	30%	177,400	22%
PM_{10}	317,600	40%	272,700	34%

Numbers rounded to nearest hundred.

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).

Table 6
Sensitivity analyses of attributable number of cases.

Sensitivity analysis of attributable number of cases								
	Concentration response function							
	Year 2000			Year 2010				
	LL	M	UL	LL	M	UL		
NO_2	79,900	175,600	227,200	52,000	119,200	158,000	LL	Incidence rate
	95,100	**209,100**[a]	270,400	61,900	**141,900**[a]	188,100	M	
	109,500	240,900	311,500	71,400	163,500	216,700	UL	
$PM_{2.5}$	79,500	207,600	304,000	59,000	159,800	241,600	LL	
	94,700	**247,100**[a]	361,900	70,300	**190,200**[a]	287,600	M	
	109,100	284,700	416,900	80,900	219,100	331,300	UL	
PM_{10}	133,500	278,200	377,900	111,700	240,700	335,800	LL	
	158,900	**331,200**[a]	449,900	133,000	**286,500**[a]	399,800	M	
	183,010	381,600	518,300	153,200	330,100	460,600	UL	

[a]Estimates using mean concentration-response function and mean incidence rate, as shown in (Table 4).
Dark red is the most conservative estimate, using the lower 95% CI bound for both the CRF and the incidence rate.
Dark green is the most extreme estimate, using the upper 95% CI bound for both the CRF and the incidence rate.

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 NO_2 contributes to the least burden of disease while PM_{10} 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 NO_2, between 9 and 66% of $PM_{2.5}$ and 9–53% of PM_{10} (Sundvor et al., 2012). Hence, NO_2, 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 NO_2 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 NO_2 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 NO_2 in urban areas as compared to rural areas, as shown in Table S2. This contrast was not as great for $PM_{2.5}$, which had only a 4% and 2% absolute difference in percent of asthma incident cases between urban and rural locations, while PM_{10} 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

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 NO_2 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 NO_2. In their follow-up study, Khreis et al. (2018b) reported that the $PM_{2.5}$, PM_{10} 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 parse 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 generations, 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 PM_{10}, stationary sources accounted for 90% of emissions and $<2\%$ were from on-road sources, while for $PM_{2.5}$, 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 NO_2 and $PM_{2.5}$, 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 ($\approx 80\%$).

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 (NO_2, $PM_{2.5}$, and PM_{10}) 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 NO_2, suggesting that NO_2 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., 2000; 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 NO_2, $PM_{2.5}$, and PM_{10} 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 $PM_{2.5}$ and PM_{10}, 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).

Funding

This research was made possible by funding from the Texas A&M Transportation Institute's (TTI) Center for Advancing Research in Transportation Emissions, Energy, and Health (CARTEEH), a U.S. Department of Transportation's University Transportation Center with the grant number (69A3551747128). Part of this publication was also developed under the Center for Clean Air Climate Solutions (CACES), which was supported under Assistance Agreement No. R835873 awarded by the U.S. Environmental Protection Agency. It has not been formally reviewed by EPA. The views expressed in this document are solely those of authors and do not necessarily reflect those of the Agency. EPA does not endorse any products or commercial services mentioned in this publication.

Disclaimer

The contents of this report reflect the views of the authors, who are responsible for the facts and the accuracy of the information presented herein. This document is disseminated in the interest of information exchange. The report is funded, partially or entirely, by a grant from the U.S. Department of Transportation's University Transportation Centers Program. However, the U.S. Government assumes no liability for the contents or use thereof.

Acknowledgments

We would like to thank Dr. Inyang Uwak for her assistance in proofreading the manuscript and Dr. Dan Seedah for his help in setting up the online website for the interactive maps and tables. Raed Alotaibi also would like to thank Amal Almutairi for her continuous support.

Competing financial interests

The authors declare they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2019.03.041.

References

Anderson, H., Favarato, G., Atkinson, R., 2011. Long-term exposure to outdoor air pollution and the prevalence of asthma: meta-analysis of multi-community prevalence studies. Air Qual. Atmos. Health 6, 57–68.

Anderson, H.R., Favarato, G., Atkinson, R.W., 2013. Long-term exposure to air pollution and the incidence of asthma: meta-analysis of cohort studies. Air Qual. Atmos. Health 6, 47–56.

Bechle, M.J., Millet, D.B., Marshall, J.D., 2015. National spatiotemporal exposure surface for NO_2: monthly scaling of a satellite-derived land-use regression, 2000–2010. Environ. Sci. Technol. 49, 12297–12305.

Beckerman, B., Jerrett, M., Brook, J.R., Verma, D.K., Arain, M.A., Finkelstein, M.M., 2008. Correlation of nitrogen dioxide with other traffic pollutants near a major expressway. Atmos. Environ. 42, 275–290.

Beelen, R., Hoek, G., Pebesma, E., Vienneau, D., De Hoogh, K., Briggs, D.J., 2009. Mapping of background air pollution at a fine spatial scale across the European Union. Sci. Total Environ. 407, 1852–1867.

Blackwell, D., Vickerie, J., Wondimu, E., 2003. Summary health statistics for US children: national health interview survey, 2000. In: Vital Health Stat. National Center for Health Statistics.

Bloom, B., Cohen, R., Freeman, G., 2011. Summary health statistics for U.S. children: National Health Interview Survey, 2010. In: Vital Health Stat. National Center for Health Statistics.

BUREAU, U.C., 1994. Geographic Areas Reference Manual.

Castro-Rodríguez, J.A., Holberg, C.J., Wright, A.L., Martinez, F.D., 2000. A clinical index to define risk of asthma in young children with recurrent wheezing. Am. J. Respir. Crit. Care Med. 162, 1403–1406.

CDC, 2009. Centers for Disease Control and Prevention. Behavioral Risk Factor Surveillance System Survey Data. 2019 U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, Georgia.

CDC, 2010. Asthma Severity among Children with Current Asthma.

CDC, 2011. Centers for Disease Control and Prevention. 2006–2008 ACBS Summary Data Quality Report. 2011.
Clark, L.P., Millet, D.B., Marshall, J.D., 2017. Changes in transportation-related air pollution exposures by race-ethnicity and socioeconomic status: outdoor nitrogen dioxide in the United States in 2000 and 2010. Environ. Health Perspect. 125, 1–10.
EPA, 2014. 2014 National Emissions Inventory report. [Online]. Available. https://gispub.epa.gov/neireport/2014/, Accessed date: 25 January 2019.
Global Asthma Network, 2014. The Global Asthma Report 2014.
Gowers, A.M., Cullinan, P., Ayres, J.G., Anderson, H.R., Strachan, D.P., Holgate, S.T., Mills, I.C., Maynard, R.L., 2012. Does outdoor air pollution induce new cases of asthma? Biological plausibility and evidence; a review. Respirology 17, 887–898.
Health Effects Institute, H. E. I, 2010. Traffic-related air pollution: a critical review of the literature on emissions, exposure, and health effects, special report 17. In: HEI Panel on the Health Effects of Traffic-Related Air Pollution. Health Effects Institute, Boston, Massachusetts (2010).
Hystad, P., Setton, E., Cervantes, A., Poplawski, K., Deschenes, S., Brauer, M., Van Donkelaar, A., Lamsal, L., Martin, R., Jerrett, M., 2011. Creating national air pollution models for population exposure assessment in Canada. Environ. Health Perspect. 119, 1123.
Joe, C., Bhaskar, K., Yihui, X., 2018. Leaflet: Create Interactive Web Maps With the JavaScript 'Leaflet' Library, 2.0.1 ed. .
Karner, A.A., Eisinger, D.S., Niemeier, D.A., 2010. Near-roadway air quality: synthesizing the findings from real-world data. Environ. Sci. Technol. 44, 5334–5344.
Khreis, H., Kelly, C., Tate, J., Parslow, R., Lucas, K., Nieuwenhuijsen, M., 2017. Exposure to traffic-related air pollution and risk of development of childhood asthma: a systematic review and meta-analysis. Environ. Int. 100, 1–31.
Khreis, H., De Hoogh, K., Nieuwenhuijsen, M.J., 2018a. Full-chain health impact assessment of traffic-related air pollution and childhood asthma. Environ. Int. 114, 365–375.
Khreis, H., Ramani, T., DE Hoogh, K., Mueller, N., Rojas-Rueda, D., Zietsman, J. & Nieuwenhuijsen, M. J. 2018b. Traffic-related air pollution and the local burden of childhood asthma in Bradford, UK. Int. J. Transp. Sci. Technol.
Kim, S.-Y., Bechle, M., Hankey, S., Sheppard, L., Aa, S., Marshall, J.A., 2019. Parsimonious Approach for Estimating Ambient Concentrations of Criteria Pollutants in the Contiguous U.S. (in prep).
Kirkwood, B., Sterne, J., 2003. Essentials of Medical Statistics. Blackwell Science, Malden, MA.
Kravitz-Wirtz, N., Teixeira, S., Hajat, A., Woo, B., Crowder, K., Takeuchi, D., 2018. Early-life air pollution exposure, neighborhood poverty, and childhood asthma in the United States, 1990–2014. Int. J. Environ. Res. Public Health 15.
Krzyzanowski, M., Cohen, A., 2008. Update of WHO air quality guidelines. Air Qual. Atmos. Health 1, 7–13.
Manson, S., Schroeder, J., Van Riper, D., Ruggles, S., 2017. PUMS National Historical Geographic Information System: Version 12.0 [Database]. University of Minnesota, Minneapolis (2017).
Martinez, F.D., 2007. Genes, environments, development and asthma: a reappraisal. Eur. Respir. J. 29, 179–184.
McConnell, R., Berhane, K., Yao, L., Jerrett, M., Lurmann, F., Gilliland, F., 2006. Traffic, susceptibility, and childhood asthma. Environ. Health Perspect. 114, 766–772 (Find this article online).
Monn, C., 2001. Exposure assessment of air pollutants: a review on spatial heterogeneity and indoor/outdoor/personal exposure to suspended particulate matter, nitrogen dioxide and ozone. Atmos. Environ. 35, 1–32.
Moorman, J.E., Akinbami, L.J., Bailey, C., Zahran, H., King, M., Johnson, C., Liu, X., 2012. National surveillance of asthma: United States, 2001–2010. In: Vital & Health Statistics. Series 3, Analytical and Epidemiological Studies, pp. 1–58.
Mueller, N., Rojas-Rueda, D., Basagaña, X., Cirach, M., Cole-Hunter, T., Dadvand, P., Donaire-Gonzalez, D., Foraster, M., Gascon, M., Martinez, D., 2017. Urban and transport planning related exposures and mortality: a health impact assessment for cities. Environ. Health Perspect. 125, 89.
National Heart Lung and Blood Institute, 2007. National Asthma Education and Prevention Program. Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma: Full Report 2007.
Novotny, E.V., Bechle, M.J., Millet, D.B., Marshall, J.D., 2011. National satellite-based land-use regression: NO_2 in the United States. Environ. Sci. Technol. 45, 4407–4414.
Nurmagambetov, T., Kuwahara, R., Garbe, P., 2018. The economic burden of asthma in the United States, 2008–2013. Ann. Am. Thorac. Soc. 15, 348–356.
Perez, L., Künzli, N., Avol, E., Hricko, A.M., Lurmann, F., Nicholas, E., Gilliland, F., Peters, J., McConnell, R., 2009. Global goods movement and the local burden of childhood asthma in southern California. Am. J. Public Health 99, S622–S628.
Perez, L., Declercq, C., Iñiguez, C., Aguilera, I., Badaloni, C., Ballester, F., Bouland, C., Chanel, O., Cirarda, F.B., Forastiere, F., Forsberg, B., Haluza, D., Hedlund, B., Cambra, K., Lacasaña, M., Moshammer, H., Otorepec, P., Rodríguez-Barranco, M., Medina, S., Künzli, N., 2013. Eur. Respir. J. 42, 594–605. https://doi.org/10.1183/09031936.00031112.
R Core Team, 2018. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing.
Richmond-Bryant, J., Saganich, C., Bukiewicz, L., Kalin, R., 2009. Associations of $PM_{2.5}$ and black carbon concentrations with traffic, idling, background pollution, and meteorology during school dismissals. Sci. Total Environ. 407, 3357–3364.
Rowangould, G.M., 2013. A census of the US near-roadway population: public health and environmental justice considerations. Transp. Res. Part D: Transp. Environ. 25, 59–67.
Ryan, P.H., Lemasters, G.K., Biswas, P., Levin, L., Hu, S., Lindsey, M., Bernstein, D.I., Lockey, J., Villareal, M., Hershey, G.K.K., 2007. A comparison of proximity and land use regression traffic exposure models and wheezing in infants. Environ. Health Perspect. 115, 278.
Sundvor, I., Balaguer, N.C., Viana, M., Querol, X., Reche, C., Amato, F., Mellios, G., Guerreiro, C., 2012. Road traffic's contribution to air quality in European cities. In: ETC/ACM Technical Paper 2012/14 November 2012. The European Topic Centre on Air Pollution and Climate Change Mitigation (ETC/ACM) (a Consortium of European Institutes under Contract of the European Environment Agency).
US Census Bureau, 1994. Geographic Areas Reference Manual.
US Census Bureau, 2010. American Factfinder. US Census Bureau, Washington, DC.
Vienneau, D., De Hoogh, K., Bechle, M.J., Beelen, R., Van Donkelaar, A., Martin, R.V., Millet, D.B., Hoek, G., Marshall, J.D., 2013. Western European land use regression incorporating satellite-and ground-based measurements of NO2 and PM10. Environ. Sci. Technol. 47, 13555–13564.
Wenzel, S.E., 2012. Asthma phenotypes: the evolution from clinical to molecular approaches. Nat. Med. 18, 716.
Werk, L.N., Steinbach, S., Adams, W.G., Bauchner, H., 2000. Beliefs about diagnosing asthma in young children. Pediatrics 105, 585–590.
WHO, 2005. Air Quality Guidlines Global Update 2005.
Winer, R.A., Qin, X., Harrington, T., Moorman, J., Zahran, H., 2012. Asthma incidence among children and adults: findings from the behavioral risk factor surveillance system asthma call-back survey—United States, 2006–2008. J. Asthma 49, 16–22.
Zahran, H.S., Bailey, C.M., Damon, S.A., Garbe, P.L., Breysse, P.N., 2018. Vital signs : asthma in children — United States, 2001–2016. MMWR Morb. Mortal. Wkly Rep. 67, 149–155.
Zhou, Y., Levy, J.I., 2007. Factors influencing the spatial extent of mobile source air pollution impacts: a meta-analysis. BMC Public Health 7, 89.