Executive summary of Report #1

Asthma is the most common chronic lung disease in childhood, around 6 million children in the US are affected by asthma. It is well established that exposure to ambient air pollution can lead to exacerbations of asthma, however, there is debate over whether ambient air pollution initiates asthma. New emerging evidence is suggestive that traffic related air pollution increases the risk of developing asthma. Two meta-analysis papers have found a positive association between exposure to traffic related air pollution and increase incidence of asthma. Anderson et al. (2013) in a meta-analysis that included 17 cohort studies reported a positive association between pollutants from traffic sources (NO2) and asthma incidence, while another meta-analysis by Khreis et al. (2017) also found a positive association between black carbon, NO2, PM2.5 and PM10 and childhood incidence and or prevalence. Advancements in biotechnology has increased our understanding of the complex disease pathways of asthma, in particularly how environmental and genetic factors interact resulting in different endotypes of asthma that might explain how the development of asthma is associated with the environment. In light of this new evidence we aim to estimate the burden of disease for childhood asthma attributable to the exposure to traffic related air pollution using an attributable fraction model, in which we estimate the number of new cases of asthma that are caused by exposure to traffic related air pollution.

Exposure to traffic related air pollution will be assessed by estimating NO2 levels at the geographic centroid location of each census block level in the whole continental US for the years 2000 and 2010. NO2 is a good predictor for traffic related air pollution sources and studies have shown that it is associated with multiple adverse health outcomes including asthma. Estimates of NO2 levels will be provided at the geographical centroid of the census blocks using a satellite derived land use regression model developed by Bechle et al. (2015). The model uses both satellite data sources and EPA monitor readings of NO2 levels and incorporates several covariates including Impervious surfaces, elevation, major roads, residential roads, and distance to coast which make up the "Spatial" component of the model. The "Spatial" component is then scaled with a "Temporal" component through adding average monthly monitor readings for 11 years, resulting in a "Spatiotemporal" model which has a high accuracy of prediction with a R^2 range of (0.63 – 0.82). The benefits of using Bechle's LUR is that measurements are provided at a continental scale with readings covered for all available census blocks, temporal scalability is incorporated to the model giving monthly average reading for 11 consecutive years, and a high accuracy reaching an R^2 of 0.82 for predicting NO2 levels at unmeasured locations. Average NO2 levels for the whole U.S. have been dropping (9.69 ppb – 6.32 ppb) from 2000 to 2010 consecutively, all the states within the U.S. has seen a decline in average NO2 levels during the same time period. District of Columbia had the highest average reading compared to other states for 2000 (20.49 ppb) which dropped to (14.12 ppb) in 2010, while the state with the lowest average NO2 level in 2000 was North Dakota (3.17 ppb) which also dropped to (2.42 ppb) in 2010. We also report each states median, mean, absolute change and relative change of average NO2 levels in the report.

Census data was obtained from the National Historical Geographic Information System (NHGIS). We only included the 48 states for the contiguous US and the District of Columbia. Alaska, Hawaii and Puerto Rico were excluded since exposure data was not available for these locations. The US Census Bureau uses a geographical hierarchical framework for census purposes in the form of States, Regions, Divisions, States, Counties, Census Tracts, Block Groups and Census Blocks, respectively. Demographic characteristics that we will use includes population counts <18 years and race which are available at the census block level, while ethnicity, income, poverty, education, employment are available at the block group level.

Report #1 to the Center for Advancing Research in Transportation Emissions, Energy, and Health (CARTEEH)

Project Title: Traffic-Related Air Pollution and Childhood Asthma in the United States: A Burden of Disease Assessment

Authors: Haneen Khreis, PhD

Raed Alotaibi, MD

Project Background

Asthma is a chronic airway disease characterized by episodes of coughing, shortness of breath and wheezing. Worldwide, asthma is conservatively estimated to effect more than 334 million people (Global Asthma Network, G, 2014), with varying degrees of intensity (Wenzel et al. 2009). Around 6 million children in the United States are affected by asthma, making the condition the most common chronic lung disease in childhood (The Lancet 2018).

Asthma has a complex causal pathway in which multiple genetic and environmental factors interact, however the causal pathways of asthma are still not completely understood (Martinez 2007). It is well established that asthma can be exacerbated by exposure to ambient air pollution of varying concentrations and sources (World Health Organization 2005). These exacerbations occur across a variety of outcomes such as increasing rates of hospitalizations, emergency room visits and medication used (Schildcrout et al. 2006; Schwartz et al. 1993; Gauderman et al. 2002; Sunyer et al. 1997; Lierl and Hornung 2003; Lipsett et al. 1997; Von Klot et al. 2002; Slaughter et al. 2003). There is, however, debate over whether air pollution can initiate asthma. Previous studies have shown that exposure to general ambient air pollution is not associated with the initiation of new cases of asthma (Anderson et al. 2011). New evidence, however, suggests an association between exposure to a more specific type of air pollution, most notably, traffic-related air pollution and an increase in new asthma cases (Anderson et al. 2013; Khreis et al. 2017).

In light of this new evidence, we aim to estimate the burden of disease for childhood asthma attributable to the exposure to traffic-related air pollution (TRAP). A full project work plan has been already submitted and approved by CARTEEH. Henceforward, the reports submitted, including this report, will focus on describing the work completed to date, and give clear account of the methodologies adopted to ensure the work is replicable and rigorous. Further, project results will be described as they emerge.

In this report, we will give a summary of the evidence suggesting an association between TRAP and new cases of childhood asthma by presenting: 1) the biological plausibility of this association and 2) the exposure-response functions and their significance. We will review the burden of disease estimation model and discuss some papers that applied it. We will then discuss the method we will use to estimate the exposure of interest and compare it different modeling techniques We will present the exposure data collated and analyzed to date. Finally, we will overview the census data and underlying definitions, in preparation for the next steps. As such, this report presents Tasks #1 and #2 as identified in the submitted and approved project work plan. It also provides background and underlying definitions in preparation for Task#3 as identified in the submitted and approved project work plan.

TRAP and New Cases of Childhood Asthma: The Evidence

A. Biological Plausibility

Asthma is a complex disease with a complex causal pathway (Martinez 2007). The complexity of asthma can be seen through its various phenotypes and endotypes which can be characterized by the different triggering factors, clinical presentations, pathological features, disease severity and responsiveness to treatment, to name a few (Corren 2013). Advancement in biological techniques has given us a better understanding how different genetic and environmental factors interact resulting in the different endotypes (Wenzel et al. 2009; Mauad et al. 2007; Holgate 2007; Tgavalekos et al. 2007; Holgate et al. 2000). In particular, advances in genetic techniques showed a wide range of biological mechanisms in which groups of genes control different pathways that result in the susceptibility to the development of asthma. For example, certain groups of genes control airway development, repair and remodeling while another group of genes control the level of response of the immune system to different triggering factors (Martin 2008; Holgate et al. 2007; Nadeem et al. 2008; Ober et al. 2011) Interactions between genes and environmental factors have been proposed as potential mechanisms that may explain the development of asthma in association with the environment. Some mechanisms include damage to the airways from pollutants through oxidative stress depleting anti-oxidants in the airways, pollutants interacting with airway walls resulting in airway remodeling, influencing the expression of inflammatory mediators and enhancing respiratory sensitization to allergens (Gowers et al. 2012).

B. Significance of the Association

Studies examining the association between ambient air pollution at the community level and incidence of asthma concluded that there is no association. A meta-analysis of cross sectional studies by Anderson et al. (2011) which included 21 studies examining the community level concentrations of multiple air pollutants (NO_2, PM_{10}, Ozone and Sulphur dioxide) found no association with asthma prevalence at the community's level. However, studies that examined air pollution levels that were associated with traffic sources showed positive and statistically significant associations with asthma incidence and prevalence. A more recent meta-analysis by Anderson et al. (2013) of cohort studies included 17 studies examining within-community exposure contrasts dominated by traffic pollution found that NO_2, but not $PM_{2.5}$, levels had a significant association with asthma incidence. Another meta-analysis by Khreis et al. (2017) examined the associations between TRAP and childhood asthma incidence or lifetime prevalence as addressed in case control, cohort, and cross-sectional studies. The meta-analysis included 41 studies and found positive and statistically significant associations between black carbon, NO_2, $PM_{2.5}$ and PM_{10} and childhood asthma incidence and/or prevalence.

Burden of Disease Estimation Model and Implications/ Future Application Possibilities

The public health and policy relevance of the positive and statistically significant associations between TRAP and childhood asthma onset are largely unknown as the impact of TRAP exposures on the burden of childhood asthma onset or prevalence is poorly documented. Due to the ubiquity of TRAP and the high number of exposed children, the relatively small individual risks of TRAP-associated asthma could translate into significant public health impacts with significant health care costs. Yet, this deduction is unconfirmed and is contested as supporting evidence and calculations are scarce.

To estimate the burden of childhood asthma in association with TRAP within the Contiguous United States, we will use standard risk assessment methods that have been previously applied in the context of childhood asthma (Künzli 2008; Perez et al. 2009; Perez et al. 2012; Perez et al. 2013). The aim is to estimate how many new (i.e. incident) childhood asthma cases can be attributable to the exposure of interest, on an annual basis. The attribution of incident asthma cases to TRAP has substantial implications for the burden of asthma-related exacerbations as well. As air pollution increases the risk of developing new asthma cases, then all future acute exacerbations of these cases, regardless of subsequent (immediate) causes of the exacerbations, should be again attributed to air pollution. This is a conceptual model which has been suggested by Nino Künzli (Künzli 2008) and is illustrated in Figure 1 below.

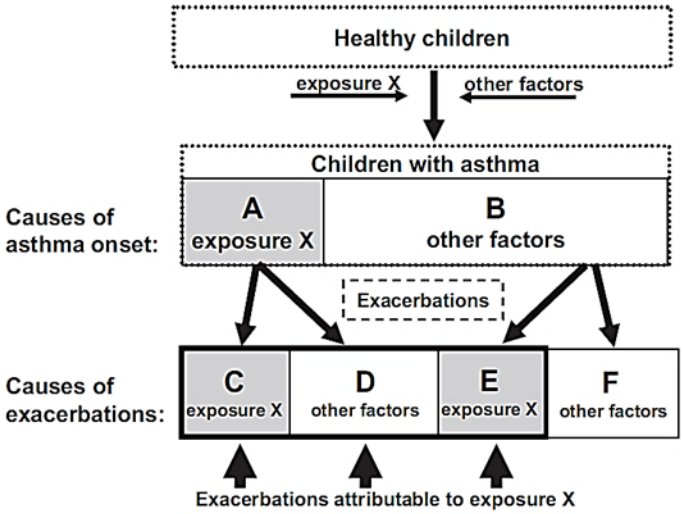

Figure 1. The burden of asthma exacerbations in children attributable to "exposure X," assuming a causal role of X in both disease onset and exacerbation. Source: Künzli et al. (2008).

Sizes of the boxes do not reflect the burden. The model starts with healthy children where some develop asthma due to X (A) or due to other causes (B). If X was the cause of asthma onset (A), all exacerbations among group A could be attributed to this factor X (C + D). Ambient air pollution is an example for "exposure X".

The model illustrated in Figure 1 expands on traditional risk assessment methods. Traditional methods attribute the exacerbations of chronic diseases to exposures of interest that directly induce the episode of exacerbation [direct], while not accounting for episodes of exacerbations induced by different exposures that occur among cases with underlying chronic disease caused by exposure of interest [indirect]. On the other hand, the conceptual model shown in Figure 1 accounts for both [direct] and [indirect] induction of exacerbations. When this model is followed, the burden of disease estimates associated with air pollution are revised to account not only for asthma symptoms that are directly triggered by air pollution (Boxes C and E in Figure 1); but also for asthma symptoms triggered by other causes in children who developed asthma *because* of air pollution (**Error! Reference source not found.** D in Figure 1). As such, traditional risk assessment methods underestimate the health impacts of exposures that do have a role in the causal pathway of chronic disease

Certain assumptions are accepted when using the expanded model (Figure 1), first, that the exposure has a causal role in the disease development, second, that the exposure has a causal role in the disease exacerbations, and third, that those with the disease due to the exposure wouldn't have developed the disease without the exposure. Whilst we focus on the estimation of Boxes A and B in this project, we pave the way forward for future analysis aiming at estimating boxes C, D, E and F.

Exposure Assessment Air Pollution Land-Use Regression Modelling – First Principles

Land-use regression modelling (LUR) is a commonly used empirical-statistical method in air pollution epidemiology. The method has become widely used for estimating within-urban variability in air pollution, typically associated with traffic emissions (Bechle et al. 2015, Anderson et al. 2013). The method uses least squares regression to combine measured pollutant concentrations with geographical information system (GIS) -based predictor data reflecting pollutant sources and surrounding land use characteristics to build a prediction model applicable to non-measured locations (Khreis and Nieuwenhuijsen, 2017). The general pros and cons of LUR models, in comparison to other exposure models, have been previously described in Khreis and Nieuwenhuijsen (2017), and are summarized in Table 1.

Table 1. Pros and cons of exposure assessment methods used in TRAP and asthma research. TRAP: traffic-related air pollution. Source: Khreis and Nieuwenhuijsen (2017)

Exposure Model	Resolution		Specificity to Traffic	Pros	Cons
	Spatial	Temporal			
TRAP surrogates main e.g., proximity to "major roads" or "freeways"	-	--	+	Intuitive, simple and cost effective, more insightful when complemented with vehicle counts and composition, low need for updated data.	Assumes a road of a certain type or size corresponds to a certain amount of traffic, sometime uses self-reported traffic intensity (collected via questionnaires) which can be subjective, assumes all pollutants disperse similarly (limited directional dependence), cannot consider street canyon effects, generally does not consider compounded effects of proximity to multiple roads, disregards exposure variability due to mobility/individual activity.
Air pollutants measurements from fixed-site monitoring stations	--	++	--	High and continuous temporal resolution, actual measurements rather than predictions, cost-effective, can provide large sample sizes, medium need for updated data.	Not present at all locations, locations usually based on regulatory (not scientific) purposes, cannot consider street canyon effects (unless located in a street canyon), conceals persons' differences because of a mismatch between data used to estimate exposure and actual subjects' locations, potential for significant amounts of missing data in practice, quality of the data depends on quality of data ratification and verification, disregards exposure variability due to mobility/individual activity.
Air pollutant measurements from residential (stationary) samplers	++	-	-	Provides individualized data, captures spatial variability in exposure between study subjects, actual measurements rather than predictions, cost effective for select pollutants (e.g., NO_2), medium need for updated data.	Only practical/ feasible in small timeframes and populations, logistic and costs concerns, not available or cost prohibitive (e.g., ultra-fine particles) for all pollutants of concern, disregards exposure variability due to mobility/individual activity.
Remote sensing	+	-	--	Can provide estimate for large areas, can provide estimate areas where measurements or models are not available (e.g., low income countries), relatively standardized method across regions, medium need for updated data.	Availability depends on satellite presence (i.e., time resolution is limited), crude spatial resolution (10 * 10 km), only available for select pollutants, challenging to assess errors in estimates, cannot consider street canyon effects, disregards exposure variability due to mobility/individual activity.

Land-use regression models	+	--	+	Assume independence between sampled locations, good agreement between measured and predicted averages of NO_2, less with PM, modelling based on measurements and information around measurement points, relatively easy to collate input data, practical, low costs, medium need for updated data.	Only reflect the predictors used in the model, subject to varying uncertainties amongst different pollutants, the true contribution of traffic to the regression is not always known or reported, difficult to take into account street canyon effects; meteorology and atmospheric chemistry, the quality of the data representing "meaningful" predictors may be an issue and will affect the overall accuracy of the model, the model's outputs are sensitive to the locations and density of the sampling sites, generally disregards exposure variability due to mobility/individual activity.
Air dispersion models	++	++	++	Continuous exposure metric, traffic-specific i.e., based on traffic flows and flow mix, traffic emissions, meteorology and atmospheric chemistry, covers relatively large areas, can assess episodic short-term and long-term exposures, can consider street canyon effects through optional built-in street canyon model, considers compounded effects of proximity to multiple roads, medium need for updated data.	Severe data demands, resource intensive, at the mercy of the emission factors inputted in the model (subject to high uncertainty), meteorology at the exposure scale is influenced by complex physical features including traffic turbulence which is difficult to consider, overestimates pollution levels during periods of calm wind, generally disregards exposure variability due to mobility/individual activity.

Air Pollution Land-Use Regression Modelling – US Model Adopted

In this project, we adopt the US-wide LUR model developed by Bechle et al. (2015) to estimate the annual 2000 and 2010 NO_2 levels at the centroid location of the census block: the smallest geographical entity publicly available for census data collection. NO_2 is a good predictor for traffic related air pollution sources, and studies have associated NO_2 pollution with multiple adverse health outcomes including asthma and asthma exacerbations (Anderson et al 2011, Anderson et al 2013, Khreis et al 2017). A brief description of the model developed by Bechle et al. (2015) is given below. The results of the model are discussed in the section after. Bechle et al (2015) developed an improved NO_2 LUR model for the Contiguous United States, mainly using Satellite and EPA monitor based measurements of NO2. In this work, we are interested in their models for years 2000 and 2010, as these years have complete decennial census data that we link the exposure data to. The LUR models developed in their work are an expansion of previously developed LUR model in the year 2006, for ground level NO_2 for the Contiguous United States. Enhanced features of their 2006 model compared to typical LUR models include:

- Broad geographic coverage, covering the continental U.S.
- Inclusion of (rather than newly collected measurements):
  - Satellite derived estimates of ground level NO_2
  - Regulatory monitoring data

- Greater temporal coverage and precision

The model building was divided into two parts, building the "Spatial" model which included spatial covariates and adding on the "Temporal" component which included temporal scaling of the spatial model. The land-use covariates that were included to build the base model were six and are shown in Table 2 below, and the final base "Spatial" model is shown in Table 3 below. The validation of the spatial model was satisfactory achieving an R^2 = (0.5-0.81) in hold-out cross-validation, check Table 4 below. The spatial model had an excellent spatial resolution typical for urban-scale LURs (~100 m scale) and covered 100% of US Census blocks.

Table 2 Independent Variables Used for Model Building†, Source: Bechle et al. (2015)

Parameter	Units	Spatial resolution	Buffer‡ or point estimate
Impervious surface [a]	%	1,000 m	buffer
Tree canopy [b]	%	500 m	buffer
Population [c]	#	1 km	buffer
Major road length [d]	m	NA	buffer
Minor road length [d]	m	NA	buffer
Total road length [d]	m	NA	buffer
Elevation [e]	m	90 m	Point
Distance to coast [f]	m	NA	point
DOMINO NO2 [g]	ppb	13 × 24 km2 at nadir	point

†Data sources: a (Elvidge et al. 2007), b: (DeFries et al. 2000), c: (Center for International Earth Science Information Network 2005), d: (2009 US Census Tiger), e: (Jarvis et al. 2008), f: (ESRI ArcGIS), g: (Bechle et al. 2013). ‡Buffers employed (m): 100; 200; 300; 400; 500; 600; 700; 800; 1000; 1200; 1500; 1800; 2000; 2500; 3000; 3500; 4000; 5000; 6000; 7000, 8000; 10000. (adapted from Novotny et al. 2011)

The temporal component added on the spatial model was used to derive other year's exposure surfaces including 2000 and 2010. The scaling to the other years was done using temporal scaling factors established from NO_2 monthly mean concentrations from EPA monitors in the contiguous US, for the respective years. For each monitor to be used, it should have at least 75% of the hourly values. Adding temporal scalability to the spatial model made the models in terms of accuracy (R^2 = 0.63-82), check Table 5 below. Models were evaluated using R^2 and Adjusted R^2, mean error and absolute error, mean bias and absolute bias. Results for the final model are shown in (Table 4 & 5). Sensitivity analysis was done using a Monte Carlo random sampling approach to explore the model stability as a function of the number of training locations used for model building using random subsets of monitoring data and each subset running 500 iterations (figure 2). The R^2 of Bechle's LUR model is consistent with other continental-scale NO2 models; Novotny et al (2011) reported US National NO2 LUR with an R2 = 0.78, Haystaf et al (2011) reported Canadian National NO2 with an R2 = 72%, Beelen et al (2009) reported EU NO2 with an R2 = 61%, Vienneau et al (2013) reported Western Europe NO2 with an adjusted R2 = 58%.

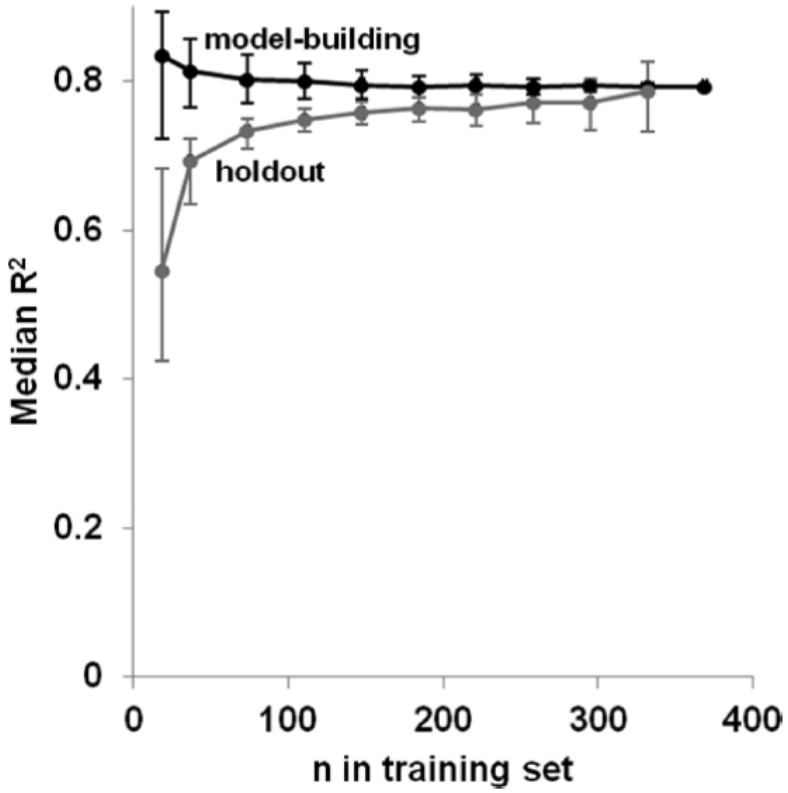

Figure 2 – Median and interquartile range R^2 for Monto Carlo random sampling, Source: Bechle et al. (2015)

Table 3 Final Model Using the Traditional LUR Approach, Source: Bechle et al. (2015)

Parameter	Units	β	std error	p > |t|	Partial R2	IQR	β × IQR
Intercept	ppb	2.44	0.41	<0.01			
DOMINO + WRF-Chem NO2	unitless	0.72	0.036	<0.01	0.62	6.3	6
Impervious (800 m)	%	0.085	0.0094	<0.01	0.75	43	4.9
Elevation (truncated)	km	11.1	0.17	<0.01	0.76	0.27	1.9
Major roads (800 m)	km	0.3	0.056	<0.01	0.78	3.2	0.91
Residential roads (100 m)	km	2.82	1.04	0.01	0.78	0.27	0.77
Distance to coast	km	-1.2×10^{-3}	3.8×10^{-4}	<0.01	0.79	630	−0.72

Table 4 Model Performance for Final Spatial LUR Model, Source: Bechle et al. (2015)

	R^2	adj R^2	Mean error (ppb)	Mean abs error (ppb)	Mean bias (%)	Mean abs bias (%)
All	0.79	0.79	−0.30	2.3	18	34
Urban	0.76	0.76	−0.78	2.4	−1	18
Rural	0.5	0.49	0.39	2.4	57	75
Population-weighted	0.81	0.81	−0.71	2.4	−1	17

Table 5 Summary of Monthly Mean NO2 Estimates Using Kriging Temporal Scaling (2000-2010), Source: Bechle et al. (2015)

	Mean spatial R2	Mean temporal R2	Spatio-temporal R2	Mean conc. (ppb)	Mean error (ppb)	Mean abs error (ppb)	Mean bias (%)	Mean abs bias (5)
All								
Population- weighted	0.82	0.76	0.85	19.6	−0.3	2.7	2	18
unweighted	0.81	0.73	0.84	12.4	−0.05	2.4	21	38
Urban classification								
urban	0.76	0.76	0.8	16.2	−0.5	2.7	1	20
suburban	0.76	0.76	0.81	13.6	−0.02	2.4	6	22
rural	0.63	0.63	0.69	6	0.4	2	78	95

Using land use regression model for exposure assessment has several limitations. The exposure model assumes that NO2 exposure is from ambient outdoor air pollution but does not take into account ambient indoor air pollution, for example how much exposure is from indoor NO2 levels. It also assumes that NO2 exposure is form one single location and does not take into account time-activity patterns, for example how much of the exposure happens at school or at the playground. Another limitation is exposure misclassification error, the precision of the LUR model varies within urban areas although it has spatiotemporal predictive pattern of (R^2 = 0.61-0.79), leading to misclassification of exposure in either direction depending the direction of error of the NO2 prediction, for example if the model is over predicting this will lead to overexposure classification but if the model is under predicting the opposite might be true.

Land-Use Regression Modelling – Exposure Estimates

Matthew Bechle from the University of Washington, has run the final LUR model and estimated the annual 2000 and 2010 NO_2 concentrations at the centroid location of the census block (the smallest geographical entity publicly available for census data collection). We categorized and analyzed this data, which we will use as the basis for our exposure assessment, and we present the results of this analysis below. NO2 levels dropped between the years 2000 and 2010 in the whole of the US and across all the 48 states and D.C. with a national mean and median difference of 35% check Figures 2-5. District of Columbia had the highest NO2 levels compared to other states, in 2000 the mean NO2 level was 20.49 ppb which dropped to 14.12 ppb in 2010 with and absolute difference of 6.37 ppb and a 31% reduction while North Dakota was the lowest state with mean NO2 levels in 2000 of 3.17 ppb which dropped to 2.42 ppb. The state with the highest absolute mean NO2 level difference between 2000 and 2010 was New Jersey of 6.73 ppb (17.49 to 10.73 ppb) while the state with the highest percent mean change of NO2 levels between 2000 and 2010 was Florida with a 43.2% reduction in mean NO2 levels (9.16 to 5.2 ppb) check (table 6). The population weighted NO2 levels were also estimated using the following formula

$$\text{Population weighted NO2} = \sum(\text{NO2 levels at census block centroid} * \text{population at census block}) / \sum(\text{population at census block})$$

For year 2000 the population weighted average NO2 levels was 14.12 ppb, while for 2000 the level was 8.86 ppb. The results of the population weighted NO2 levels for both years are similar to the results from Clark et al (2017).

Table 6 Annual 2000 and 2010 NO_2 Concentrations (ppb) at the Census Block Centroid across the Contiguous United States

States	Median				Mean			
	Y2000	Y2010	Diff	%change	Y2000	Y2010	Diff	%change
United States	8.19	5.29	-2.90	-0.35	9.69	6.32	-3.37	-0.35
Alabama	7.52	4.80	-2.73	-0.36	8.44	5.26	-3.18	-0.38
Arizona	7.93	5.51	-2.42	-0.31	10.71	7.26	-3.46	-0.32
Arkansas	5.42	3.92	-1.50	-0.28	6.29	4.54	-1.75	-0.28
California	13.87	8.52	-5.35	-0.39	16.20	9.88	-6.32	-0.39
Colorado	9.40	6.18	-3.21	-0.34	11.55	8.10	-3.45	-0.30
Connecticut	13.19	7.83	-5.36	-0.41	13.67	8.20	-5.47	-0.40
Delaware	8.90	6.10	-2.80	-0.31	10.44	6.99	-3.46	-0.33
District of Columbia	19.82	13.73	-6.09	-0.31	20.49	14.12	-6.37	-0.31
Florida	8.71	4.86	-3.85	-0.44	9.16	5.21	-3.95	-0.43
Georgia	7.40	4.83	-2.57	-0.35	8.25	5.42	-2.83	-0.34
Idaho	5.30	3.52	-1.78	-0.34	6.39	4.23	-2.16	-0.34
Illinois	11.55	7.57	-3.98	-0.34	13.74	9.47	-4.27	-0.31
Indiana	12.02	7.29	-4.74	-0.39	12.97	7.97	-5.00	-0.39
Iowa	5.21	3.93	-1.28	-0.25	6.16	4.65	-1.51	-0.25
Kansas	5.55	3.89	-1.65	-0.30	6.57	4.68	-1.89	-0.29
Kentucky	8.79	5.50	-3.29	-0.37	10.08	6.32	-3.76	-0.37
Louisiana	5.73	3.68	-2.05	-0.36	7.42	4.69	-2.73	-0.37
Maine	4.94	2.88	-2.06	-0.42	5.33	3.11	-2.22	-0.42
Maryland	11.24	7.62	-3.63	-0.32	11.95	8.19	-3.76	-0.31
Massachusetts	11.19	6.68	-4.51	-0.40	12.17	7.27	-4.90	-0.40
Michigan	8.02	5.32	-2.70	-0.34	9.54	6.33	-3.21	-0.34
Minnesota	5.04	3.55	-1.50	-0.30	6.73	4.79	-1.94	-0.29
Mississippi	5.37	3.56	-1.81	-0.34	6.25	4.14	-2.11	-0.34
Missouri	5.85	4.18	-1.66	-0.28	6.66	4.71	-1.95	-0.29
Montana	3.67	2.36	-1.31	-0.36	4.14	2.71	-1.43	-0.35
Nebraska	4.91	3.32	-1.58	-0.32	5.98	4.08	-1.90	-0.32
Nevada	6.71	5.08	-1.63	-0.24	8.55	6.43	-2.12	-0.25
New Hampshire	7.63	4.35	-3.29	-0.43	8.33	4.74	-3.60	-0.43
New Jersey	16.82	10.28	-6.54	-0.39	17.49	10.76	-6.73	-0.38
New Mexico	5.64	4.44	-1.20	-0.21	6.77	5.31	-1.46	-0.22
New York	10.87	6.05	-4.83	-0.44	14.23	8.31	-5.91	-0.42
North Carolina	8.19	5.33	-2.87	-0.35	8.72	5.66	-3.06	-0.35
North Dakota	2.47	1.93	-0.54	-0.22	3.17	2.42	-0.75	-0.24
Ohio	11.33	6.92	-4.41	-0.39	12.13	7.41	-4.72	-0.39
Oklahoma	5.94	4.22	-1.73	-0.29	7.01	5.00	-2.01	-0.29
Oregon	6.30	3.95	-2.35	-0.37	7.86	4.92	-2.95	-0.37
Pennsylvania	12.95	7.82	-5.13	-0.40	13.96	8.51	-5.46	-0.39
Rhode Island	11.86	7.04	-4.82	-0.41	12.17	7.18	-4.99	-0.41
South Carolina	6.55	4.40	-2.15	-0.33	7.09	4.77	-2.32	-0.33
South Dakota	2.91	1.99	-0.92	-0.32	3.64	2.47	-1.18	-0.32

Tennessee	9.11	5.80	-3.32	-0.36	10.01	6.59	-3.42	-0.34
Texas	6.42	4.57	-1.85	-0.29	7.64	5.52	-2.12	-0.28
Utah	6.98	4.93	-2.05	-0.29	9.38	6.60	-2.78	-0.30
Vermont	7.06	4.19	-2.87	-0.41	7.30	4.32	-2.97	-0.41
Virginia	8.74	5.94	-2.80	-0.32	9.99	6.81	-3.18	-0.32
Washington	8.73	6.31	-2.42	-0.28	10.17	7.34	-2.84	-0.28
West Virginia	9.24	6.03	-3.21	-0.35	9.91	6.45	-3.46	-0.35
Wisconsin	6.58	4.37	-2.21	-0.34	7.79	5.21	-2.58	-0.33
Wyoming	3.99	2.48	-1.51	-0.38	4.92	3.03	-1.89	-0.38

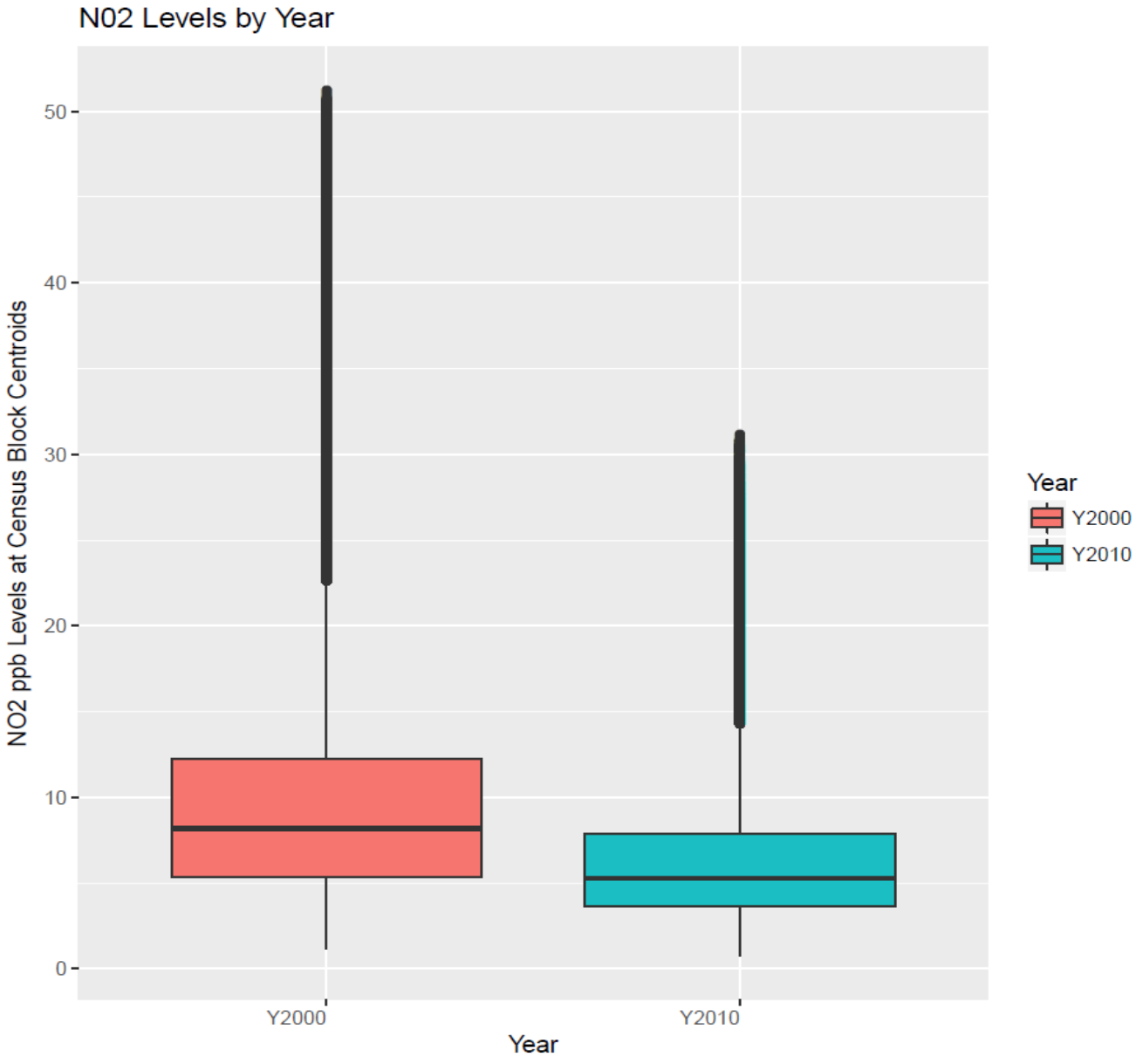

Figure 2 –National Annual NO2 ppb Concentrations at the Census Block Centroid for the Years 2000 and 2010

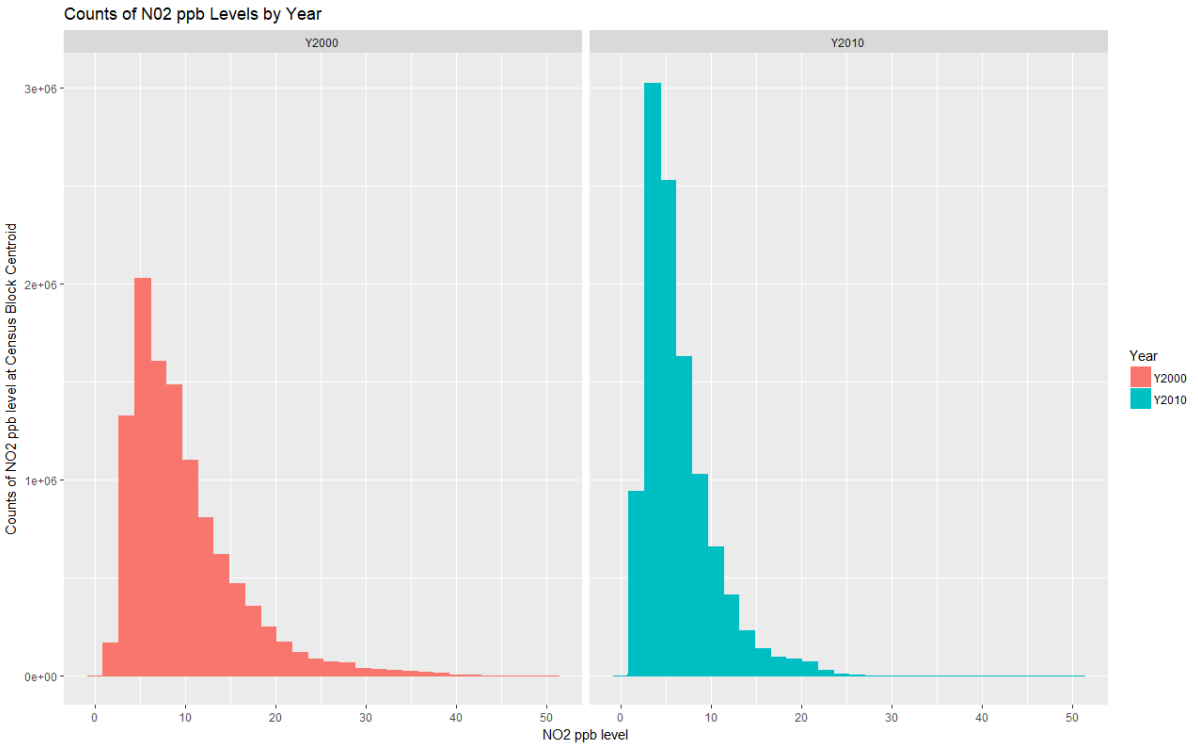

Figure **3** – **National Annual NO2 ppb Concentrations at the Census Block Centroid for the Years 2000 and 2010**

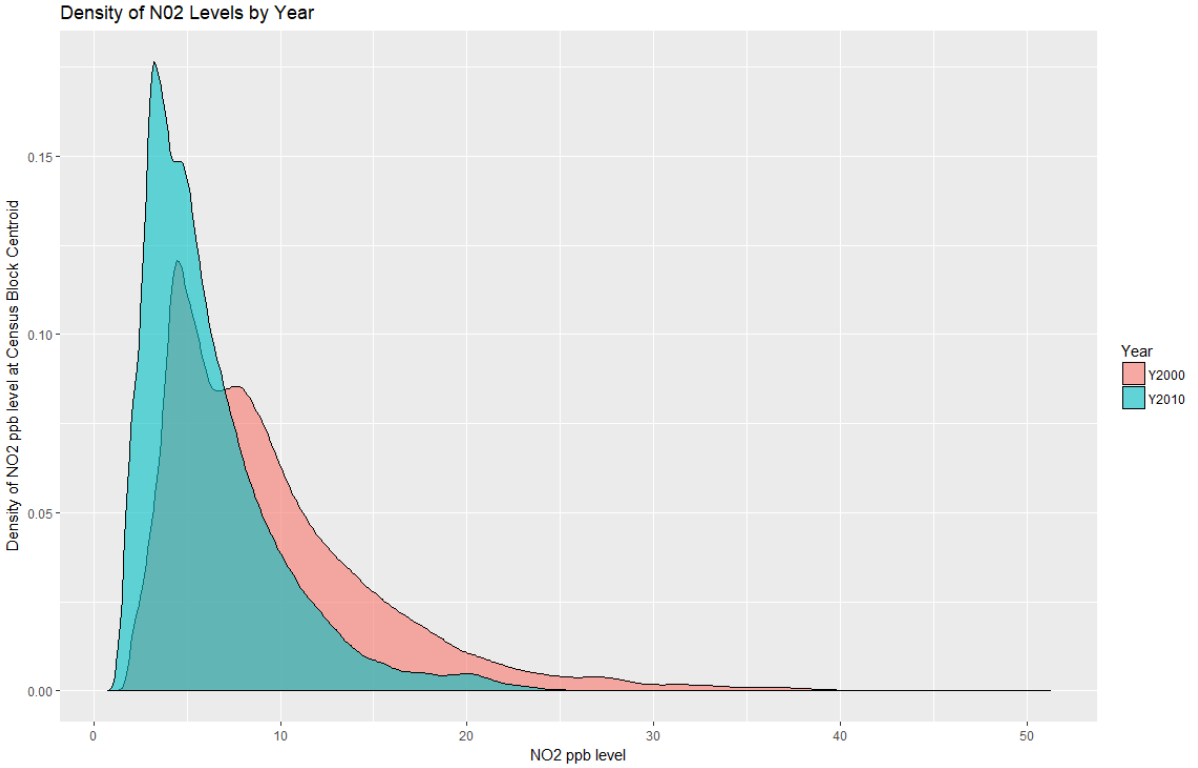

Figure **4** – **National Annual NO2 ppb Concentrations at the Census Block Centroid for the Years 2000 and 2010**

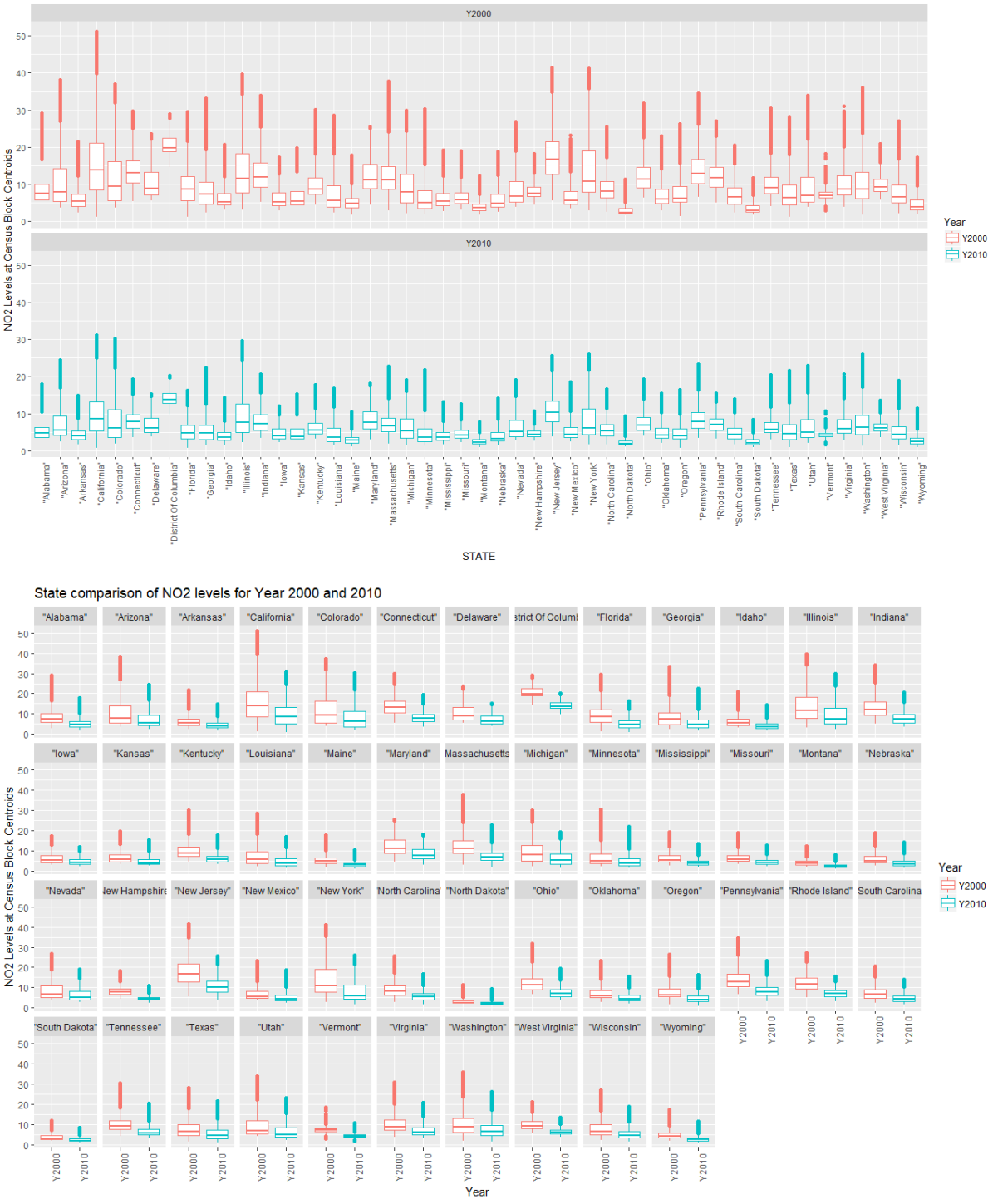

Figure 5 – Annual NO2 ppb Concentrations at the Census Block Centroid for the Years 2000 and 2010 for the 48 U.S. States and D.C separately.

In preparation for Task #3, an exploration of the US census data and its geographical coverage and hierarchy was undertaken and is reported below. The information below is intended to serve as a reference for others wanting to work with census data in the future.

The census data that was downloaded from the National Historical Geographic Information System (NHGIS) website https://www.nhgis.org/ https://www.nhgis.org/ for the 48 states and the District

of Columbia (excluding Hawaii, Alaska and Puerto Rico), also known as the Contiguous United States. Air pollution data from the LUR models described above were not available for Alaska, Hawaii and Puerto Rico, and hence these states were excluded from our analysis, also in line with previous analysis (Clark et al. 2017). We are currently looking at two years for analysis: 2000 and 2010. The total population in the included census blocks in 2000 and 2010 are shown in Table 6.

Table 6 Total US population (48 states + DC)

	Y2000	Y2010
Total Population count	279,583,437	306,675,006
population count < 18 years old		
Number of census blocks	8,164,718	11,007,989

The smallest geographical entity for which the Census Bureau collects population counts is the census block level. Census blocks nest within all other tabulated census geographic entities and forms the basis for all tabulated data (see Figure). This is the geographical level that we will use for our analysis when available i.e. attributing asthma cases to air pollution.

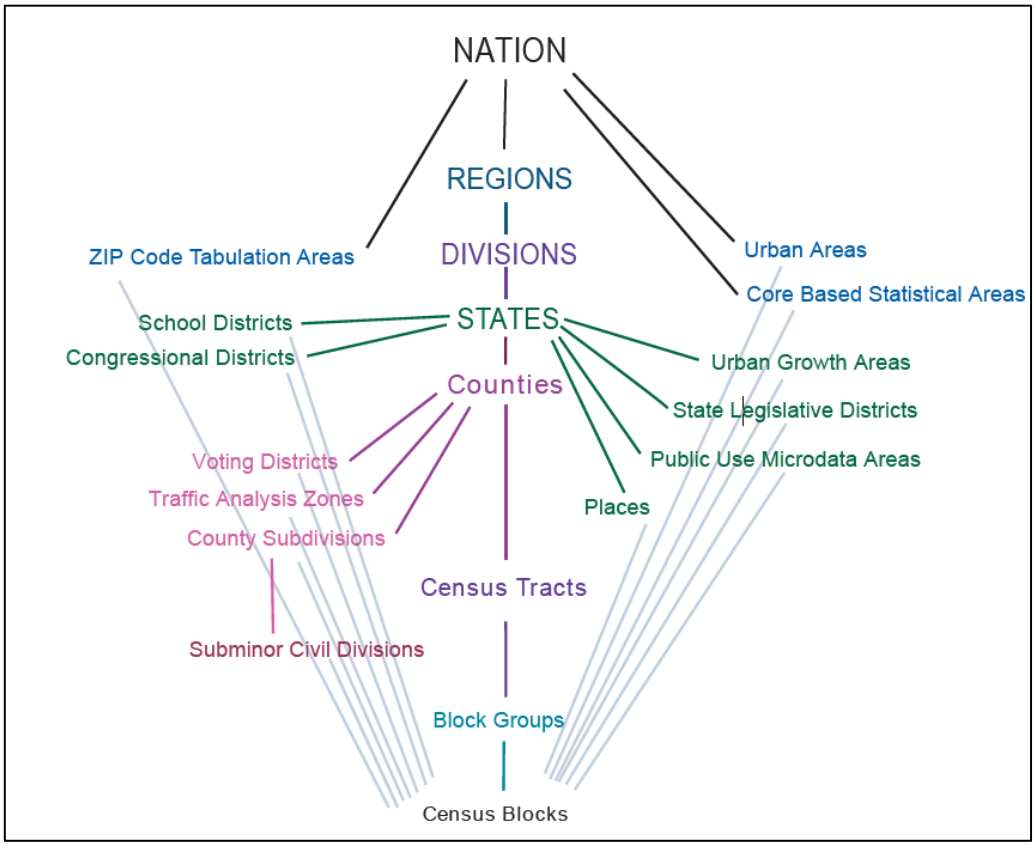

Figure 6 Standard Hierarchy of Census Geographic Entities in the US, Source: US Census Bureau

When presenting the final results, we have decided to aggregate the results from census block level and present them (in the paper and following associated reports) at the:

- County level (relevant for policy makers, local policies and legal considerations);
- State level (relevant for comparisons between states and likely matching the asthma incidence data which we hope to compile at a state level);

- Regions or Divisions level (relevant for comparisons between regions/divisions);
- Nation level (relevant to offer one national burden of disease estimate and relevant in global burden of disease estimates).

The list of the US states and their corresponding divisions (and regions) are shown in figure 7.

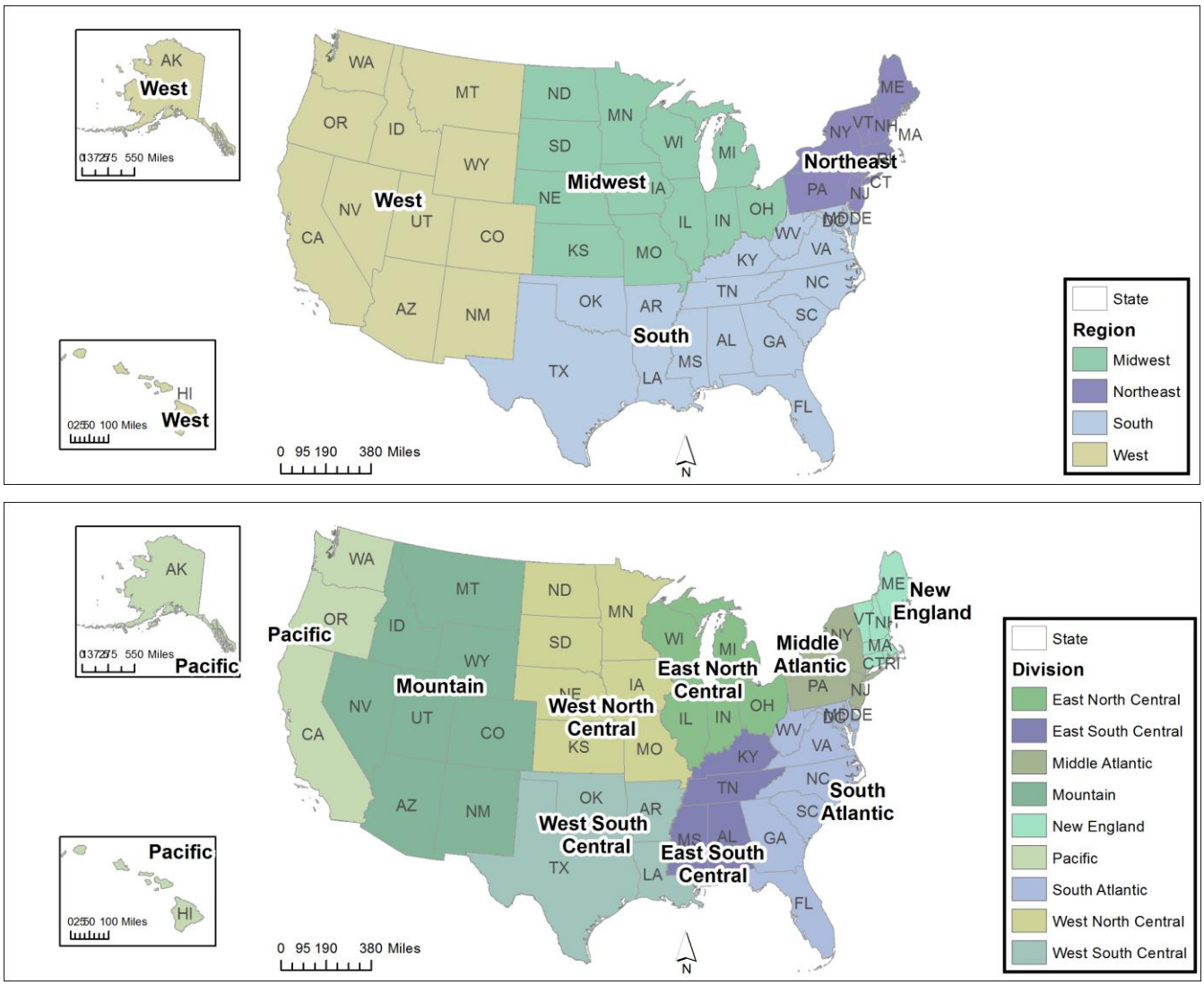

Figure 7 Census Regions and Divisions of the United States, Source: US Census Bureau

The next steps will include matching the 2000 and 2010 air pollution, childhood population count, and socioeconomic data together in one data set, for which we will produce meta-data. These data sets have different geographies which are summarized in Table 7**.**

Table 7 The different datasets we aim to compile and their geographies

Dataset	Geography
2000 NO_2 levels	Census block

2010 NO_2 levels	Census block
2000 childhood population count (< 18 years old)	Census block
2010 childhood population count (< 18 years old)	Census block
Race/ethnicity	Census block/Block group level
Income/poverty	Block group level
Education	Block group level
Employment	Block group level
Asthma incidence data	To be determined

References

Anderson HR, Favarato G, Atkinson RW. Long-term exposure to outdoor air pollution and the pervalence of asthma: meta-analysis of multi-community prevalence studies. Air Qual Atmos Heal. 2011; online pub:12 PP. https://link.springer.com/content/pdf/10.1007%2Fs11869-011-0145-4.pdf. Accessed February 14, 2018.

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 Quality, Atmosphere & Health, 6(1), 47-56. Available at: https://link.springer.com/article/10.1007%2Fs11869-011-0144-5

Bechle, M. J.; Millet, D. B.; Marshall, J. D. Remote sensing of exposure to NO2: satellite versus ground-based measurement in a large urban area. Atmos. Environ. 2013, 69 (2), 345–353.

Bechle, M.J., D.B. Millet, and J.D. Marshall, National Spatiotemporal Exposure Surface for NO2: Monthly Scaling of a Satellite-Derived Land-Use Regression, 2000–2010. Environmental science & technology, 2015. 49(20): p. 12297-12305

Center for International Earth Science Information Network (CIESIN); Gridded Population of the World Version 3 (GPWv3): Population Density Grids. Socioeconomic Data and Applications Center (SEDAC): Columbia University 2005.

Clark, L.P., D.B. Millet, and J.D. Marshall, Changes in Transportation-Related Air Pollution Exposures by Race-Ethnicity and Socioeconomic Status: Outdoor Nitrogen Dioxide in the United States in 2000 and 2010. Environmental Health Perspectives, 2017. 97012: p. 1.

Corren, Jonathan. "Asthma phenotypes and endotypes: an evolving paradigm for classification." Discovery medicine 15, no. 83 (2013): 243-249.

DeFries, R. S.; Hansen, M. C.; Townshend, J. R. G.; Janetos, a C.; Loveland, T. R. A new global 1 km dataset of percentage tree cover derived from remote sensing. Glob. Chang. Biol. 2000, 6 (2), 247–254.

Elvidge, C. D.; Tuttle, B. T.; Sutton, P. C.; Baugh, K. E.; Howard, A. T.; Milesi, C.; Bhaduri, B.; Nemani, R. Global Distribution and Density of Constructed Impervious Surfaces. Sensors 2007, 7 (9), 1962–1979.

Gauderman, W.J., et al., Association between air pollution and lung function growth in southern California children: results from a second cohort. American journal of respiratory and critical care medicine, 2002. 166(1): p. 76-84.

Global Asthma Network, G, 2014. The Global Asthma Report. 2014 Auckland, New Zealand.

Gowers AM, Cullinan P, Ayres JG, et al. Does outdoor air pollution induce new cases of asthma? Biological plausibility and evidence; A review. Respirology. 2012;17(6):887-898. doi:10.1111/j.1440-1843.2012.02195.

Holgate ST, Davies DE, Lackie PM, et al. The new millennium: The conquest of allergy Epithelial-mesenchymal interactions in the pathogenesis of asthma. J Allergy Clin Immunol. 2000;105(2):193-204. doi:10.1016/S0091-6749(00)90066-6

Holgate ST, Davies DE, Powell RM, Howarth PH, Haitchi HM, Holloway JW. Local genetic and environmental factors in asthma disease pathogenesis: Chronicity and persistence mechanisms. Eur Respir J. 2007;29(4):793-803. doi:10.1183/09031936.00087506

Holgate ST. Epithelium dysfunction in asthma. J Allergy Clin Immunol. 2007;120(6):1233-1244. doi:10.1016/j.jaci.2007.10.025

Jarvis, A.; Reuter, H. I.; Nelson, E. G. SRTM 90m Digital Elevation. 2008.

Khreis, H., & Nieuwenhuijsen, M. J. (2017). Traffic-Related Air Pollution and Childhood Asthma: Recent Advances and Remaining Gaps in the Exposure Assessment Methods. International journal of environmental research and public health, 14(3), 312.

Künzli N, Perez L, Lurmann F, Hricko A, Penfold B, McConnell R. An attributable risk model for exposures assumed to cause both chronic disease and its exacerbations. Epidemiology. 2008;19(2):179-185. doi:10.1097/EDE.0b013e3181633c2f

Künzli, N., et al., An attributable risk model for exposures assumed to cause both chronic disease and its exacerbations. Epidemiology, 2008. 19(2): p. 179-185.

Lierl, M.B. and R.W. Hornung, Relationship of outdoor air quality to pediatric asthma exacerbations. Annals of Allergy, Asthma & Immunology, 2003. 90(1): p. 28-33.

Lipsett, M., S. Hurley, and B. Ostro, Air pollution and emergency room visits for asthma in Santa Clara County, California. Environmental Health Perspectives, 1997. 105(2): p. 216.

Martin JG, Jo T. Genetic differences in airway smooth muscle function. Proc Am Thorac Soc. 2008;5(1):73-79. doi:10.1513/pats.200706-069VS

Martinez FD. Genes, environments, development and asthma: A reappraisal. Eur Respir J. 2007;29(1):179-184. doi:10.1183/09031936.00087906

Mauad T, Bel EH, Sterk PJ. Asthma therapy and airway remodeling. J Allergy Clin Immunol. 2007;120(5):997-1009. doi:10.1016/j.jaci.2007.06.031

Nadeem A, Masood A, Siddiqui N. Review: Oxidant—antioxidant imbalance in asthma: Scientific evidence, epidemiological data and possible therapeutic options. Ther Adv Respir Dis. 2008;2(4):215-235. doi:10.1177/1753465808094971

Ober C, Yao TC. The genetics of asthma and allergic disease: A 21st century perspective. Immunol Rev. 2011;242(1):10-30. doi:10.1111/j.1600-065X.2011.01029.

Perez, L., et al., Chronic burden of near-roadway traffic pollution in 10 European cities (APHEKOM network). European Respiratory Journal, 2013. 42: p. 594-605.

Perez, L., et al., Global goods movement and the local burden of childhood asthma in southern California. American Journal of Public Health, 2009. 99(S3): p. S622-S628.

Perez, L., et al., Near-Roadway Pollution and Childhood Asthma: Implications for Developing “Win–Win” Compact Urban Development and Clean Vehicle Strategies. Environmental Health Perspectives, 2012. 120(11): p. 1619.

Schildcrout, J.S., et al., Ambient air pollution and asthma exacerbations in children: an eight-city analysis. American Journal of Epidemiology, 2006. 164(6): p. 505-517.

Schwartz, J., et al., Particulate air pollution and hospital emergency room visits for asthma in Seattle. American Review of Respiratory Disease, 1993. 147(4): p. 826-831.

Slaughter, J.C., et al., Effects of ambient air pollution on symptom severity and medication use in children with asthma. Annals of Allergy, Asthma & Immunology, 2003. 91(4): p. 346-353.

Sunyer, J., et al., Urban air pollution and emergency admissions for asthma in four European cities: the APHEA Project. Thorax, 1997. 52(9): p. 760-765.

Tgavalekos NT, Musch G, Harris RS, et al. Relationship between airway narrowing, patchy ventilation and lung mechanics in asthmatics. Eur Respir J. 2007;29(6):1174-1181. doi:10.1183/09031936.00113606

The Lancet 2018. Asthma in US children, Editorial. DOI: https://doi.org/10.1016/S0140-6736(18)30258-7

Von Klot, S., et al., Increased asthma medication use in association with ambient fine and ultrafine particles. European Respiratory Journal, 2002. 20(3): p. 691-702.

Wenzel SE, Barnes PJ, Bleecker ER, et al. A randomized, double-blind, placebo-controlled study of tumor necrosis factor-α blockade in severe persistent asthma. Am J Respir Crit Care Med. 2009;179(7):549-558. doi:10.1164/rccm.200809-1512OC

World Health Organization. WHO Air Quality Guidelines for Particulate Matter, Ozone, Nitrogen Dioxide and Sulfur Dioxide. Global Update. 2005. http://apps.who.int/iris/bitstream/10665/69477/1/WHO_SDE_PHE_OEH_06.02_eng.pdf. Accessed February 14, 2018.

Novotny, E. V.; Bechle, M. J.; Millet, D. B.; Marshall, J. D. National satellite-based land-use regression: NO2 in the United States. 2011

Hystad, P.; Setton, E.; Cervantes, A.; Poplawski, K.; Deschenes, S.; Brauer, M.; van Donkelaar, A.; Lamsal, L.; Martin, R.; Jerrett, M.; et al. Creating national air pollution models for population exposure assessment in Canada. 2011

Beelen, R.; Hoek, G.; Pebesma, E.; Vienneau, D.; de Hoogh, K.; Briggs, D. J. Mapping of background air pollution at a fine spatial scale across the European Union. 2009

Vienneau, D.; de Hoogh, K.; Bechle, M. J.; Beelen, R.; van Donkelaar, A.; Martin, D. B.; Millet, D. B.; Hoek, G.; Marshall, J. D. Western European land use regression incorporating satellite- and ground-based measurements of NO2 and PM10. 2013

Steven Manson, Jonathan Schroeder, David Van Riper, and Steven Ruggles. IPUMS National Historical Geographic Information System: Version 12.0 [Database]. Minneapolis: University of Minnesota. 2017. http://doi.org/10.18128/D050.V12.0

US Census Bureau. https://www.census.gov/