Methods

In this paper, we aim to estimate the burden of childhood asthma due to NO_2 exposure using state specific asthma incidence rates and compare the change in burden estimates from those produced by Alotaibi et al. (2019) which used a country level asthma incidence rate, as is typically done in burden of disease assessment studies (Achakulwisut et al., 2019; Khreis, de Hoogh, et al., 2018; Khreis, Ramani, et al., 2018; Perez et al., 2013; Perez et al., 2009).

Study area and time point

We analyzed data for the 49 states within the contiguous United States (U.S) and the District of Columbia (D.C.) for the year 2010 at the smallest geographical unit available. Decennial population counts, Urban or rural living location and annual NO_2 concentrations were all available at the census block level. Median household income was available at the census block group level which is one level higher than the census block (US Census Bureau, 2010). Asthma incidence rates were available at the state level. NO_2 concentrations were not available for states outside the contiguous U.S. (Alaska, Hawaii and Puerto Rico), and hence they were excluded from the analysis.

Census data

We included populated census blocks of the contiguous U.S. for the year 2010, as obtained from the National Historical Geographic Information System (NHGIS) website (Manson et al., 2018; US Census Bureau, 2010). Each block included information on the total population of children <18 years, and whether the census block was designated as an urban or a rural block. Census-designated urban areas are defined by the census bureau using multiple criteria including total population thresholds, density, land use, and distance, with census blocks forming the basic geographical units of urban areas. Further, urban designated areas are classified into two subtypes; urban clusters or urbanized areas. Urban clusters have a population threshold of ≥2,500 and <50,000, while urbanized areas have a population threshold of ≥50,000 people. The median household income was divided into five categories consistent with two previous relevant publications: <$20,000, $20,000 to <$35,000, $35,000 to <$50,000, $50,000 to <$75,000 and ≥$75,000 (Alotaibi et al., 2019; Clark et al., 2017). Census blocks were than assigned a similar median household income groups of the census block group they reside under.

There were 2,686 (0.04%) census blocks with missing median income data in 2010 which were assigned as “Not defined” in the analysis of median household income. Table 1 summarizes the geographical and demographic data across all census blocks included in this analysis.

NO_2 exposure assessment

Annual average NO_2 concentrations for each populated census block were available at the centroid location for the year 2010. Concentrations were derived from a land use regression model utilizing Environmental Protection Agency (EPA), satellite data and several GIS covariates. A detailed description of the model can be found at Bechle et al. (2015). NO_2 concentrations were converted from ppb to ug/m^3 through multiplying by 1.88 (WHO, 2005).

Concentration-response function

We used a concentration-response function (CRF) of 1.05 (95% CI = 1.02-1.07) per 4ug/m^3 of NO_2. The CRF was obtained from a meta-analysis of 20 studies examining the association between exposure to traffic-related air pollution (TRAP) and risk of developing asthma among children (Khreis et al., 2017). These CRF represent data from the most up-to-date and widest analysis on traffic-related air pollution and the onset of childhood asthma, and have been used in several published peer-reviewed burden of disease assessments (Achakulwisut et al., 2019; Alotaibi et al., 2019; Khreis, de Hoogh, et al., 2018; Khreis, Ramani, et al., 2018).

Asthma incidence and prevalence rate

An incidence rate is defined as the number of new cases of a disease within a specified time period among an at-risk population (Mausner et al., 1985). To estimate the childhood asthma incidence rate, we obtained the BRFSS and ACBS child data (CDC, 2009, 2011)sets for the years 2006-2010 from the CDC website https://www.cdc.gov/brfss/ and used the methods described by Winer et al. (2012). The following variables were extracted; the state, asthma status question (BRFSS), incident status question (ACBS), and children sample weights. All analysis was conducted using R statistical software (R Core Team, 2018). States and territories not within the contiguous U.S. were excluded from the analysis, namely Alaska, Hawaii and Puerto Rico.

To determine the “Asthma status” of children, respondents to the BRFSS were asked “Has a doctor, nurse, or other health professional EVER said that the child has asthma?”, If the answer is “Yes”, the respondent is designated as “Ever asthma” and If the answer is “No”, the respondent is designated as “Never asthma”. Respondents with children designated as “Ever asthma” are requested to participate in the ACBS follow up survey. To determine the “Incident status”, respondents to the ACBS survey were 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 to the latter part of this question was “within the past 12 months”, the respondent is designated as an “Incident asthma”, other responses were not relevant to the analysis.

Each respondent (sample) from the ACBS and BRFSS is assigned a weight to adjust for the disproportionate population subgroup selection relative to the state’s population distribution, the variation in probability of selection, the actual response of each respondent, or nonresponse. Weights represents the number of children within each state, with similar characteristics to the respondent. Weights are used to convert response to questions of sampled children to population estimates. For example if respondent (X) had a weight of 150, his response to survey questions represent answers of 150 children within the state. Sum of childhood weights for the BRFSS represent the total population of children within each state, while the sum of weights for the ACBS represent the total population of children with “Ever asthma” within each state (Garbe et al., 2011; Korn et al., 2011).

“At-risk children” are then estimated by taking the weighted sum of respondents designated as “Incident asthma” and “Never asthma”:

$$At - risk\ children\ =\ Incident\ asthma\ (weighted) +\ Never\ asthma(weighted)$$

Equation 1

The asthma incidence rate is the product of weighted “Incident asthma” divided by “At-risk children”:

$$Asthma\ incdence\ rate = Incident\ asthma\ /\ At - risk\ children$$

Equation 2

The asthma prevalence rate is the product of weighted “Ever asthma” divided by the sum of weighted “Ever asthma” and “Never asthma”:

$$Asthma\ prevalence\ rate = Ever\ Asthma\ \ /\ (Ever\ asthma + Never\ asthma)$$

Equation 3

The average asthma incidence and prevalence rate across all states was estimated by taking the sum of weighted “Incident asthma” divided by the sum of “At-risk children” for the years 2006 through 2010. State-specific average estimates were obtained using similar steps for available states as previously mentioned. States that did not participate in the ACBCS during the whole period (2006-2010) were assigned the average asthma incidence and prevalence rate.

Burden of disease estimate

To estimate the burden of disease, we used a standard assessment methods described by Mueller et al. (2017) with the following steps:

Census block level at-risk children was estimated for each state by subtracting the total number children multiplied by the state-specific prevalence rate from the total children within the census block.

$$At - risk\ children\ "census\ block" = Total\ children - (Total\ children * Prevalence\ rate)$$

Equation 4

We then estimated the number of asthma cases within each census block by multiplying the state-specific childhood asthma incidence rate with at-risk children at the census block.

$$Asthma\ incident\ cases\ \text{census block} = At - risk\ children\ "census\ block" * Incidence\ rate$$

Equation 5

We then calculated the relative risk (RR_{diff}) for asthma due to exposure difference between estimated exposure levels (NO_2 concentration at the census block level) and no exposure (zero NO_2 concentration).

$$RR_{diff} = e^{((\ln(RR)\ /\ RR_{unit} * Exposure)}$$

Equation 6

Where RR is the CRF and RR_{unit} is the exposure unit (4 ug/m^3) for the CRF as extracted from Khreis et al. (2017).

The population attributable fraction (PAF) is then estimated using the following:

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

Equation 7

The attributable number of asthma incident cases (AC) was estimated by multiplying the PAF with the number of incident asthma cases at each census block. The attributable cases for each census block is then summed to get the total AC.

Results

NO2 concentrations and trends

The mean (min-max) NO_2 concentrations were 13.3 (1.5-58.3) ug/m^3 (Table 2). By living location, the mean NO_2 concentrations was highest at urbanized areas (18.4 ug/m^3) (Figure S1), while mean NO_2 concentration was highest among median income group of ≥$75,000 (16.5 ug/m^3) (Figure S2). When stratifying NO_2 concentrations of median income groups across living location, rural areas had an increasing average concentration as income increased, urban clusters has a decreasing average concentration as income increased and urban areas showed a U shaped trend (Figure S3 and Figure S4). South Dakota had the lowest mean NO_2 concentration (5.2 ug/m^3), while the District of Columbia had the highest (26.3 ug/m^3) (Table S1 and Figure S5). Figure S6 and Figure S7 demonstrates NO_2 concentrations across living location and median household income for each state.

ACBS and BRFSS results

Overall, there were 32 states with available childhood asthma incidence rates (Table 3 and Table S2). The total childhood samples included for the period (2006-2010) were 293,464 samples from the BRFSS and 16,156 samples from the ACBS. The BRFSS samples for each year ranged between 55,094 samples in 2006 and 61,862 in 2008. While the ACBS samples for each year ranged between 2,016 samples in 2006 and 4,095 in 2009.

The weighted estimates represent the childhood population counts of available states from the ACBS and the BRFSS.

The average national incidence rate for the years 2006-2010 was 12.1 per 1,000. The state of Montana had the lowest average childhood asthma incidence rate (IR = 4.3 per 1,000), while District of Columbia had the highest average childhood asthma incidence rate (IR = 17.7 per 1,000). States that did not have an incidence rate available (16 states) were assigned the average overall incidence rate of 12.1 per 1,000.

Asthma incident cases

Using state-specific asthma incidence rates the estimated number of childhood asthma incident cases were 754,893 in 2010 (Table 4). By living location, 19% lived in a rural area, while 9% and 72% lived in an urban cluster and urbanized area, respectively. The largest percentage of childhood asthma cases (28%) lived in an income block group of \$50,000 to <\$75,000, while the lowest percentage (4%) lived in the lowest income block group of <\$20,000. The state with the lowest number of estimated childhood asthma incident cases was Montana with 900 cases, while the state with the largest number was Texas with 99,100 cases (Table S3).

Attributable number of cases and fraction

On average, we estimated a total of 132,829 childhood asthma cases attributable to NO_2 exposure which accounted for 17.6% of all childhood asthma cases (Table 4). By living location, urbanized areas had the largest number of attributable cases totaling 109,581 cases and highest percentage of all asthma cases of 20.3%. Rural areas had total of 13,951 cases and accounting for the least percentage of all asthma cases with 9.8%, while urban clusters had only 9,296 cases representing 13% of all asthma cases (Figure S8). By income, \$50,000 to <\$75,000 had the largest number of cases attributable to NO_2, 37,559 cases accounting for 16.8% of all asthma cases. However, the income group with the largest percentage of asthma cases was the lowest income group <\$20,000, accounting for 20.8% of all asthma cases (Figure S9). The mean value of attributable fraction increased by income group in rural areas, decreased by income group in urban clusters and presented as a U shape in urbanized areas (Figure 2 and Figure S10).

The state with the lowest number of estimated attributable cases was Montana with 70 cases, while the state with the largest attributable cases was California with 19,200 cases. The state with the lowest attributable fraction was South Dakota (7.6%), while the state with the highest attributable fraction was District of Columbia (26.9) (Figure 3 and Table S3).

Figure 4 and Figure 5 present the distribution of attributable fraction by living location and median income group for each state. The majority of states follow a distribution similar to the national level with a few exceptions (e.g. see Arizona, Montana, Rhode Island & Wyoming).

Comparison with the main paper

Comparing total asthma cases

Using state-specific asthma incidence rates, the overall number of cases reduced by an average of 40,041 (5%) cases compared to estimates in the main paper that used a flat national asthma incidence rate (Table 4). By living location, the largest reduction was among urban clusters with a decrease of 4,204 (5.6%) cases followed by urbanized areas which reduced by 29,926 (5.2%) cases. By income group, the largest decrease in the number of cases was among the highest income groups by 13,123 (6.8%) cases, while the least decrease was among the lowest income group by 168 (0.6%) cases. The state of California had the largest decrease in numbers of total childhood asthma incident cases by 24,442 cases while the state of Texas had the largest increase in numbers by 25,019 cases (Table S3). The state of Montana had the largest percent reduction in total childhood asthma incident cases by 64.1% while the state of Texas had the largest percent increase by 33.8%.

Comparing attributable cases

The total attributable cases reduced by 9,103 (6.4%) cases when compared to the main paper (Table 4). By living location, urbanized areas had the largest reduction of 8,040 (6.8%) cases while rural areas had the least reduction by 514 (3.6%) cases attributable to NO_2 exposure. By income group, the highest income group also had the largest decrease in attributable cases by 2.994 (8.5%) and the lowest income group had the least decrease by 58 (1%) cases. The state of California had the largest decrease in attributable cases by 6,190 cases while the state of Texas had the largest increase by 3,615 cases (Table S3). The percent change in attributable number of cases across states is similar to the percent change in total childhood asthma incident cases using state-specific asthma incidence rates.

Comparing attributable fractions

The overall attributable fraction reduced 1.4% with urbanized areas having the largest reduction by 1.7% in terms of living location. In terms of income group, the largest reduction was 1.8% for both $50,000 to <$75,000 and ≥$75,000 (Table 4). The attributable fraction across states did not differ when using state specific asthma incidence rates.

Discussion (bullet points)

- Using state specific asthma incidence rates did not change the results much (within the range of the sensitivity analysis from the main paper)
- The state specific total number of asthma cases and attributable cases changed when applying state specific incidence rates
- The state-specific attributable fractions did not change. The reason is that the incident rate is applied uniformly across the state (spatially), thus the total asthma cases and total attributable cases will change with equal proportion when applying the new asthma incidence rate but not the attributable fraction. The attributable fraction is a function of CRF and exposure estimate regardless of the IR. Had we applied an incidence rate based on other factors like age, gender, race, income group, then the attributable fraction across the state would differ since the change won't in incidence rate won't be uniform within the state.
- The percentage of all asthma cases has a J shaped distribution when examining income groups. The lowest income group had the highest % then drops and rises again with the highest income group.
- Explore why the U shaped distribution is shown among attributable fraction for income groups.

Tables

Table 1: Census data description, year 2010

Geographic characteristics	**Total populated census blocks**	6,182,882
	Total census-designated urban areas	3,590,278
Demographic characteristics	**Total population**	306,675,006
	Total population of children (birth – 18)	73,690,271 (24%)
	Mean (range) number of children in census blocks	12 (0-2214)
Population of children by living location	**Rural**	13,763,183 (19%)
	Urban clusters (≥2,500 and <50,000 people)	6,994,464 (9%)
	Urbanized area (≥50,000 people)	52,932,624 (72%)
Population of children by median household income	**<$20,000**	2,614,804 (4%)
	$20,000 to <$35,000	12,770,843 (17%)
	$35,000 to <$50,000	18,573,954 (25%)
	$50,000 to <$75,000	21,953,876 (30%)
	≥$75,000	17,763,239 (24%)

Table 2: NO_2 concentration by strata

		Mean	**Min**	**25%**	**Median**	**75%**	**Max**
Total		13.2	1.5	7.9	11.4	16.6	58.3
By living location	**Rural**	8.0	1.5	6.0	7.8	9.8	37.7
	Urban cluster	12.0	1.6	9.6	11.9	14.2	35.6
	Urbanized area	18.4	2.6	13.0	17.0	22.1	58.3
By median household income	**<$20,000**	16.1	2.0	10.4	14.9	20.1	56.8
	$20,000 to <$35,000	13.2	1.6	8.1	11.7	16.7	58.3
	$35,000 to <$50,000	11.8	1.5	7.0	10.0	14.5	58.0
	$50,000 to <$75,000	12.8	1.6	7.6	10.8	15.7	55.7
	≥$75,000	16.5	2.1	10.9	14.9	20.6	55.5

Table 3: Childhood asthma survey summary

	2006	2007	2008	2009	2010	Total
BRFSS sample (weighted)	55,094 (50,674,742)	59,487 (43,661,381)	61,862 (53,327,550)	59,821 (47,747,373)	57,200 (39,975,264)	293,464
Ever asthma sample (weighted)	7,168 (6,493,224)	7,971 (5,763,409)	8,255 (7,218,400)	8,126 (6,279,938)	7,483 (5,158,455)	39,003
ACBS Sample (weighted)	2,017 ()	2,797 ()	3,924 ()	4,095 ()	2,196 ()	16,156
Incident case sample (weighted)	154 (404,276)	173 (312,917)	169 (385,818)	153 (297,546)	160 (319,743)	809
At-risk sample (weighted)	48,080 (30,825,589)	51,689 (36,050,557)	53,776 (26,491,259)	51,848 (25,942,087)	49,877 (22,900,850)	255,270
Incidence rate	13.1	8.7	14.6	11.5	14.0	12.1
Prevalence rate	12.8	13.2	13.5	13.2	12.9	
Number of states included						34

Table 4: Comparing results of the burden of disease using state-specific estimates vs original estimates

		Main results			Original results			Difference			Percentage difference		
		Incident cases	AC	AF	Incident cases	AC	AF	Incident cases	AC	AF	Incident cases	AC	AF
	Total	754,893	132,829	17.6%	794,934	141,931	17.9%	-40,041	-9,103	-0.3%	-5.0%	-6.4%	-1.4%
By living location (% of Total)	**Rural**	142,559 (19%)	13,951 (11%)	9.8%	148,470 (19%)	14,466 (10%)	9.7%	-5,911	-514	0.0%	-4.0%	-3.6%	0.4%
	Urban cluster	71,249 (9%)	9,296 (7%)	13.0%	75,453 (9%)	9,844 (7%)	13.0%	-4,204	-549	0.0%	-5.6%	-5.6%	0.0%
	Urbanized area	541,085 (72%)	109,581 (82%)	20.3%	571,011 (72%)	117,621 (83%)	20.6%	-29,926	-8,040	-0.3%	-5.2%	-6.8%	-1.7%
By median household income (% of Total)	**<$20,000**	28,039 (4%)	5,834 (4%)	20.8%	28,207 (4%)	5,892 (4%)	20.9%	-168	-58	-0.1%	-0.6%	-1.0%	-0.4%
	$20,000 to <$35,000	134,208 (18%)	24,906 (19%)	18.6%	137,765 (17%)	25,794 (18%)	18.7%	-3,558	-889	-0.2%	-2.6%	-3.4%	-0.9%
	$35,000 to <$50,000	190,481 (25%)	32,369 (24%)	17.0%	200,367 (25%)	34,549 (24%)	17.2%	-9,885	-2,180	-0.2%	-4.9%	-6.3%	-1.4%
	$50,000 to <$75,000	223,522 (30%)	37,559 (28%)	16.8%	236,827 (30%)	40,540 (29%)	17.1%	-13,305	-2,981	-0.3%	-5.6%	-7.4%	-1.8%
	≥$75,000	178,497 (24%)	32,133 (24%)	18.0%	191,621 (24%)	35,128 (25%)	18.3%	-13,123	-2,994	-0.3%	-6.8%	-8.5%	-1.8%

Figure 1: Childhood asthma incidence rate flow chart.

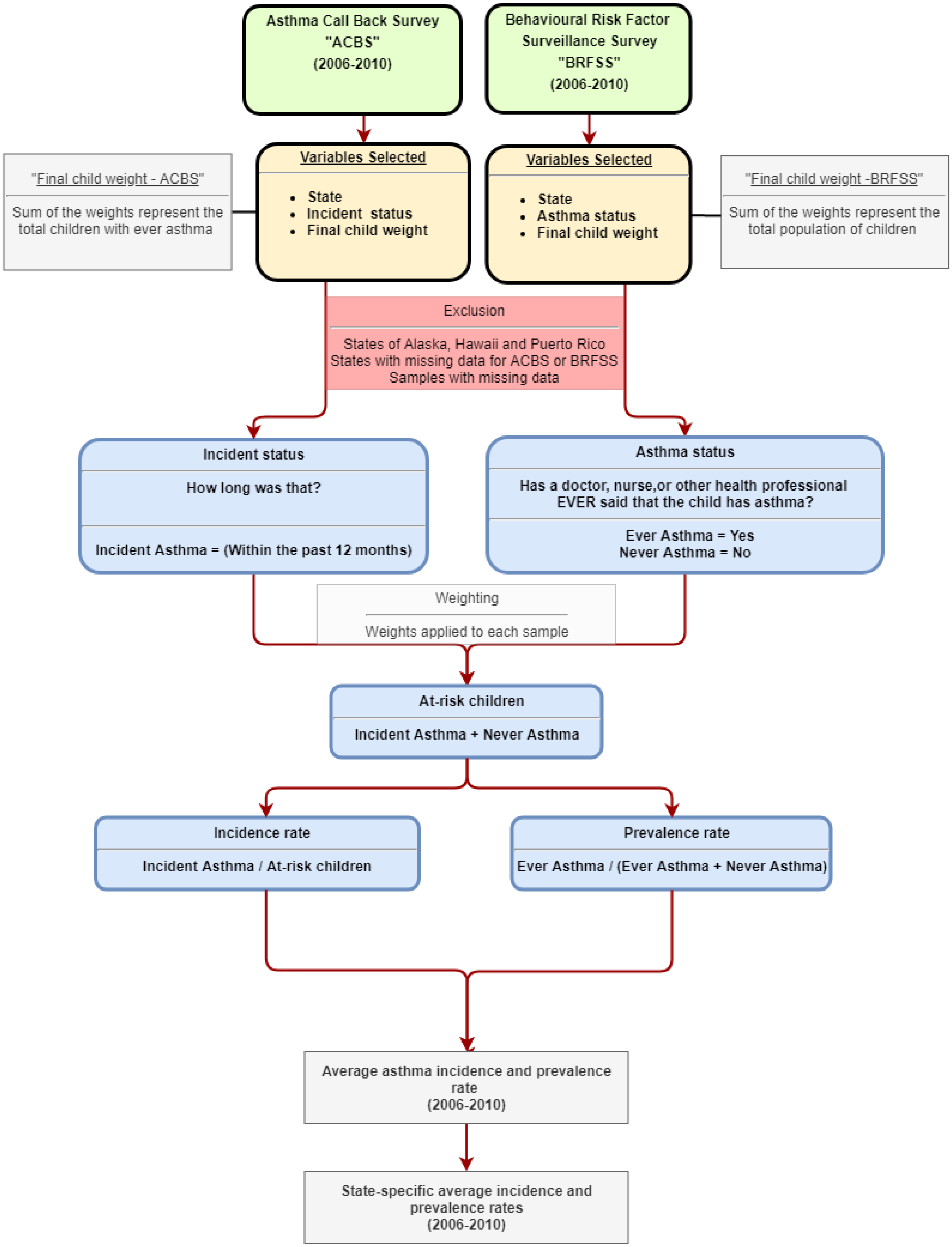


Figure 2: Attributable fraction by median income group stratified into living location

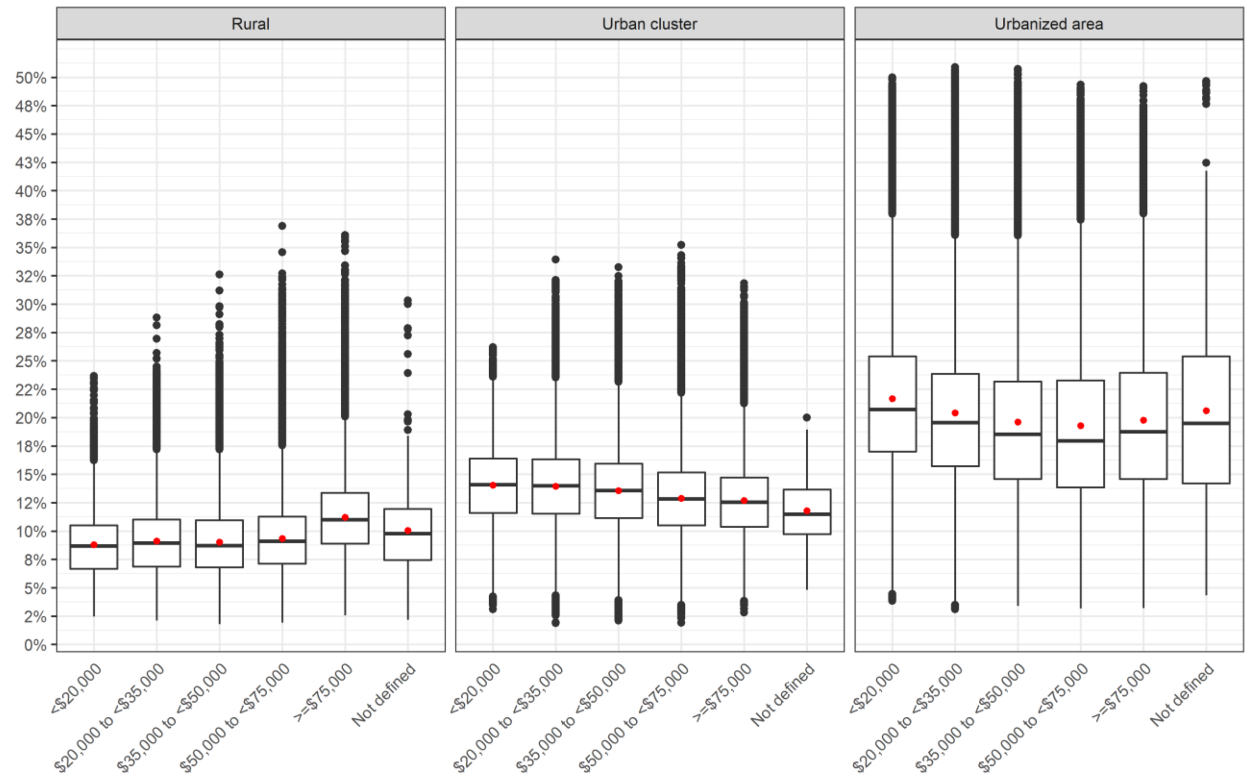


Figure 3: Attributable fraction by state

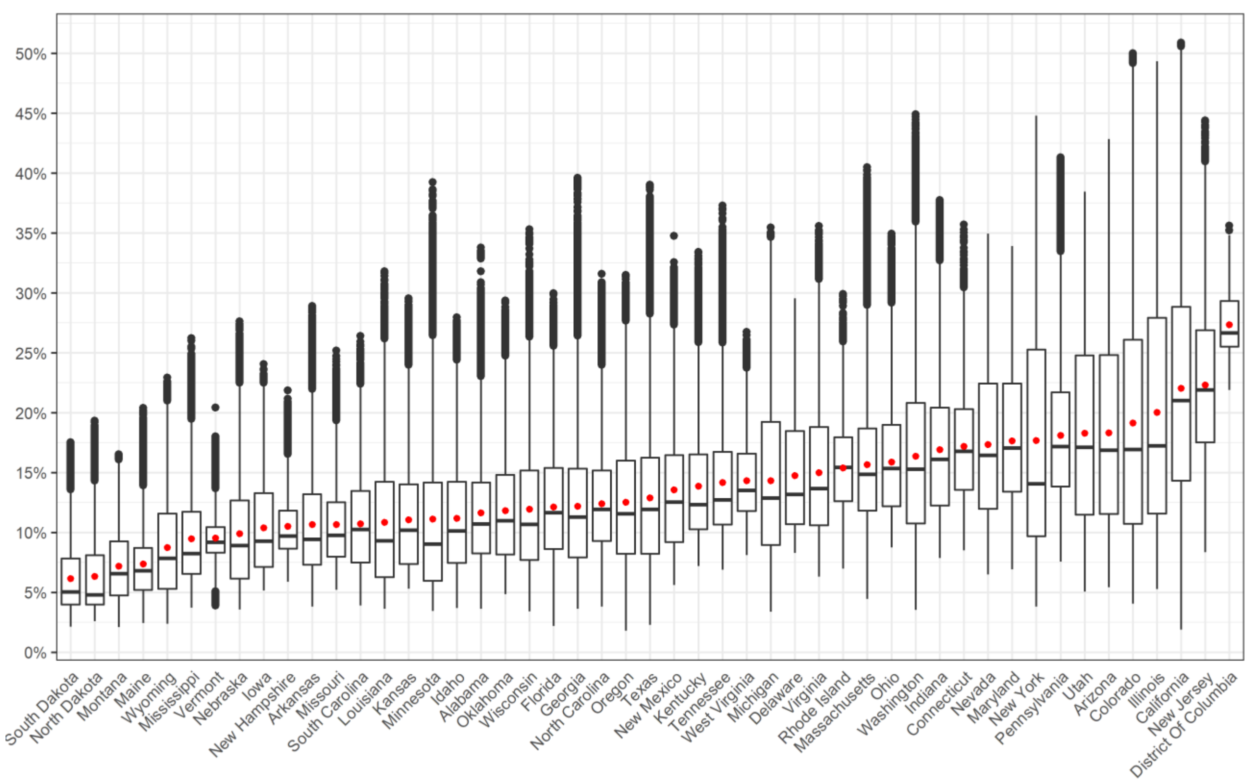


Figure 4: Attributable fraction by state and living location

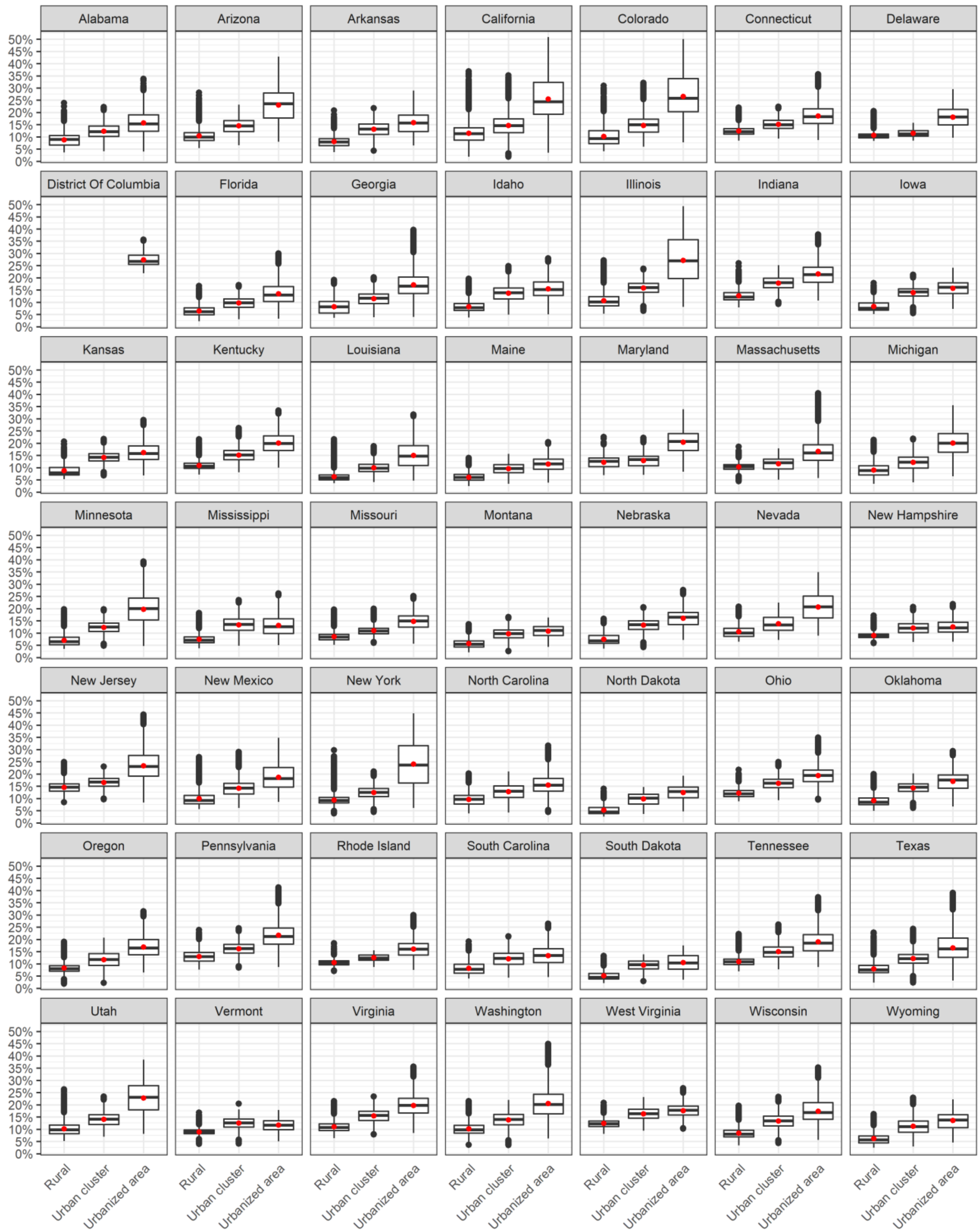
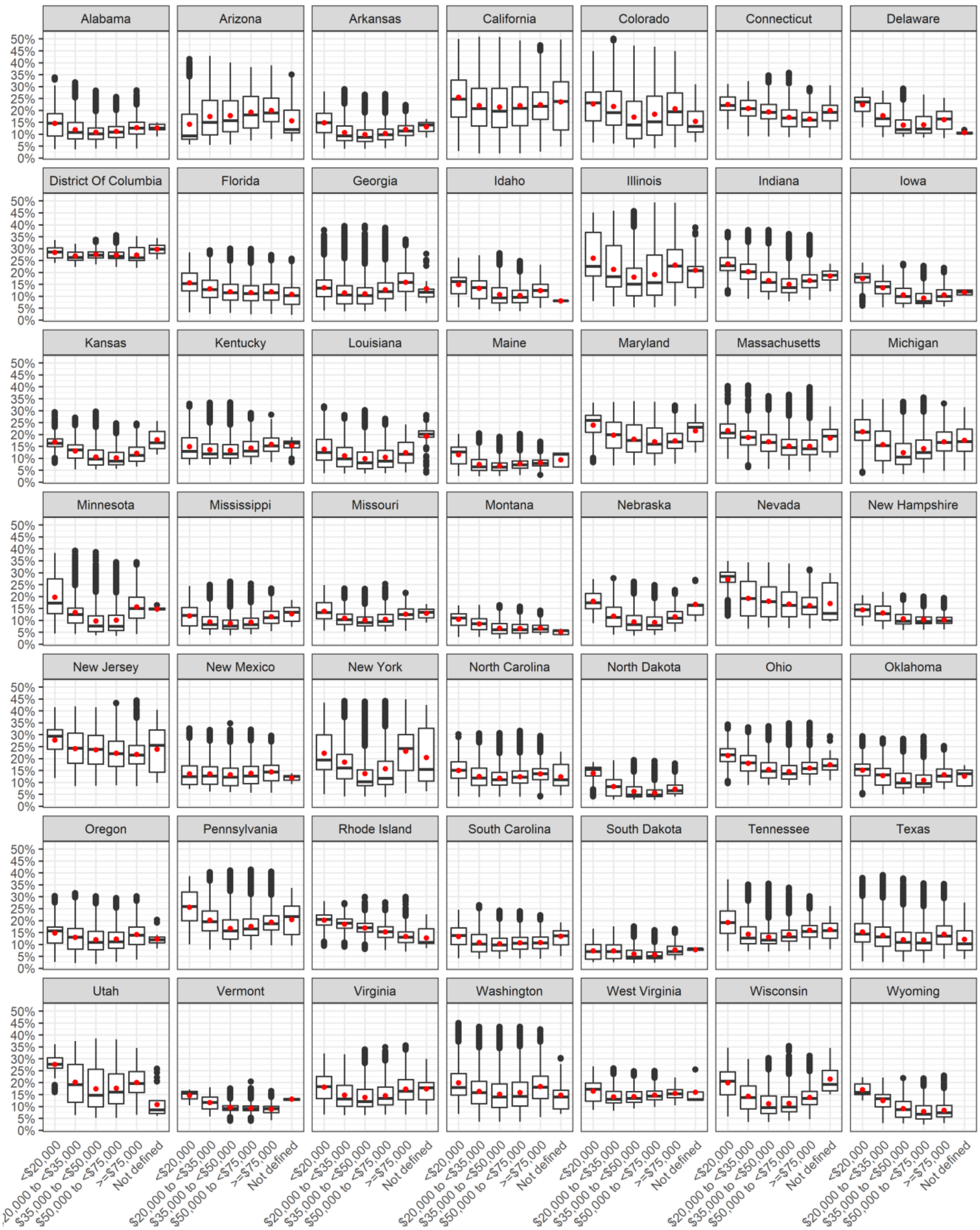


Figure 5: Attributable fraction by state and median income group



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Supplementary Material

Table S1: NO2 concentration by state

State	Mean	Min	25%	Median	75%	Max
Alabama	10.3	3.0	7.1	9.3	12.5	33.8
Arizona	17.0	4.6	10.1	15.1	23.4	45.9
Arkansas	9.3	3.2	6.2	8.1	11.6	28.0
California	21.1	1.6	12.7	19.3	27.9	58.3
Colorado	18.1	3.4	9.3	15.2	24.8	56.9
Connecticut	15.6	7.3	11.9	15.0	18.6	36.2
Delaware	13.2	7.1	9.3	11.6	16.7	28.7
District Of Columbia	26.3	20.2	24.2	25.4	28.5	36.1
Florida	10.7	1.8	7.4	10.2	13.7	29.2
Georgia	10.8	3.0	6.8	9.8	13.6	41.4
Idaho	9.8	3.1	6.4	8.8	12.6	26.9
Illinois	19.0	4.4	10.1	15.5	26.9	55.7
Indiana	15.4	6.7	10.7	14.4	18.7	38.9
Iowa	9.1	4.3	6.1	8.0	11.7	22.6
Kansas	9.7	4.5	6.3	8.8	12.4	28.7
Kentucky	12.4	6.1	8.9	10.8	14.8	33.3
Louisiana	9.6	3.0	5.3	8.0	12.6	31.4
Maine	6.3	2.0	4.4	5.8	7.5	18.7
Maryland	16.1	5.9	11.8	15.3	20.8	34.0
Massachusetts	14.1	3.7	10.3	13.2	17.0	42.5
Michigan	12.9	2.8	7.7	11.3	17.5	35.9
Minnesota	9.9	2.9	5.0	7.8	12.5	40.8
Mississippi	8.3	3.1	5.6	7.0	10.2	24.9
Missouri	9.3	4.4	6.8	8.4	11.0	23.8
Montana	6.2	1.7	4.0	5.5	8.0	14.8
Nebraska	8.6	3.0	5.2	7.7	11.1	26.5
Nevada	15.9	5.5	10.5	14.7	20.8	35.2

New Hampshire	9.1	5.0	7.4	8.4	10.3	20.2
New Jersey	21.0	7.1	15.8	20.2	25.7	48.1
New Mexico	12.1	4.7	7.9	11.0	14.8	35.0
New York	16.6	3.2	8.3	12.4	23.9	48.7
North Carolina	11.0	3.2	8.0	10.4	13.5	31.1
North Dakota	5.4	2.1	3.3	4.0	6.9	17.6
Ohio	14.3	7.5	10.7	13.6	17.3	35.2
Oklahoma	10.4	4.1	7.0	9.5	13.1	28.5
Oregon	11.1	1.5	7.0	10.1	14.3	31.0
Pennsylvania	16.6	6.4	12.2	15.5	20.1	43.7
Rhode Island	13.8	5.9	11.1	13.7	16.2	29.2
South Carolina	9.4	3.3	6.4	8.9	11.9	25.1
South Dakota	5.2	1.8	3.3	4.2	6.7	15.8
Tennessee	12.7	5.9	9.2	11.2	15.0	38.3
Texas	11.5	1.9	7.0	10.4	14.5	40.6
Utah	17.0	4.3	10.0	15.4	23.4	39.8
Vermont	8.3	3.3	7.1	7.9	9.1	18.7
Virginia	13.5	5.3	9.2	12.0	17.1	36.1
Washington	14.9	2.9	9.3	13.6	19.1	48.9
West Virginia	12.7	6.9	10.3	11.9	14.9	25.5
Wisconsin	10.6	2.8	6.6	9.3	13.5	35.7
Wyoming	7.6	2.0	4.5	6.7	10.1	21.4

Table S2: Childhood asthma survey summary by state (Total of 2006-2010)

State	ACBS Sample	BRFSS sample	Ever asthma	Incident case	At-risk	Incidence rate	Prevalence rate	Years available
Arizona	103	5,535	699	10	4,846	15.2	13.1	
California	172	11,801	1,543	13	10,271	9.3	12.2	
Connecticut	549	7,112	1,132	47	6,027	12	16	
D.C.	69	4,101	685	6	3,422	17.7	19.9	
Georgia	545	9,433	1,455	26	8,004	9.1	15.1	
Illinois	122	6,187	778	6	5,415	6.7	12.4	
Indiana	500	9,824	1,361	41	8,504	15.2	12.8	
Iowa	245	8,084	724	19	7,379	6.3	8.4	
Kansas	827	14,699	1,839	50	12,910	9	11.6	
Louisiana	88	8,829	1,214	4	7,619	5.8	13	
Maine	376	4,523	644	23	3,902	9.2	13.2	
Maryland	624	13,093	1,897	44	11,240	11.2	14.8	
Michigan	680	10,762	1,524	43	9,281	12	13.6	
Mississippi	208	10,816	1,527	14	9,303	14	14.2	
Missouri	262	5,646	814	20	4,852	12.9	13.9	
Montana	286	8,609	909	17	7,717	4.3	9.7	
Nebraska	717	17,883	1,644	53	16,292	9.1	9.3	
New Hampshire	232	5,285	664	19	4,640	12	12.1	
New Jersey	458	15,410	2,230	32	13,212	9.8	14.3	
New Mexico	287	5,554	765	17	4,806	6.7	12	
New York	404	7,083	1,079	28	6,032	14.7	15.8	
Ohio	351	7,989	1,138	32	6,883	15.1	12.3	
Oklahoma	299	8,611	1,291	21	7,341	10.8	14	
Oregon	165	4,793	579	13	4,227	11.1	11.1	

Pennsylvania	209	14,760	2,090	12	12,682	13.2	13.9	
Rhode Island	169	7,127	1,209	11	5,929	14.3	16.1	
Texas	780	16,749	2,293	55	14,511	16.6	13.1	
Utah	573	14,417	1,617	45	12,845	10.4	10.2	
Vermont	597	8,784	1,220	40	7,604	11.5	13.8	
Washington	594	9,706	1,165	33	8,574	6.8	10.8	
West Virginia	85	5,089	663	5	4,431	11.8	12.7	
Wisconsin	140	5,170	611	10	4,569	12.3	10.6	

Table S3: State results and comparison

	Main results				Comparison		Difference		
State	**Total children**	**Incident cases**	**AC**	**AF**	**Origin cases**	**Origin AC**	**Incident cases**	**AC**	**%**
Alabama	1,132,459	11,700	1,380	11.8%	12,216	1,439	-494	-58 (-4.0%)	-4.0%
Arizona	1,629,014	21,500	4,620	21.5%	17,573	3,772	3,965	851 (22.6%)	22.6%
Arkansas	711,475	7,500	860	11.6%	7,675	887	-199	-23 (-2.6%)	-2.6%
California	9,295,040	75,800	19,200	25.3%	100,270	25,395	-24,442	-6,190 (-24.4%)	-24.4%
Colorado	1,225,609	12,900	3,010	23.4%	13,221	3,089	-342	-80 (-2.6%)	-2.6%
Connecticut	817,015	8,300	1,500	18.2%	8,814	1,601	-549	-100 (-6.2%)	-6.2%
Delaware	205,765	2,000	330	16.0%	2,220	355	-184	-29 (-8.3%)	-8.3%
District Of Columbia	100,815	1,400	390	26.9%	1,088	293	346	93 (31.8%)	31.8%
Florida	4,002,091	42,100	5,360	12.7%	43,173	5,502	-1,118	-142 (-2.6%)	-2.6%
Georgia	2,491,552	19,200	2,770	14.5%	26,878	3,887	-7,713	-1,115 (-28.7%)	-28.7%
Idaho	429,072	4,700	590	12.6%	4,629	581	96	12 (2.1%)	2.1%
Illinois	3,129,179	18,300	4,510	24.7%	33,756	8,333	-15,492	-3,824 (-45.9%)	-45.9%
Indiana	1,608,298	21,300	3,850	18.1%	17,350	3,143	3,913	709 (22.6%)	22.6%
Iowa	727,993	4,200	520	12.4%	7,853	971	-3,660	-453 (-46.6%)	-46.6%
Kansas	726,939	5,800	790	13.6%	7,842	1,067	-2,061	-281 (-26.3%)	-26.3%
Kentucky	1,023,371	10,700	1,590	14.9%	11,040	1,649	-389	-58 (-3.5%)	-3.5%
Louisiana	1,118,015	5,600	650	11.6%	12,061	1,401	-6,445	-749 (-53.4%)	-53.4%
Maine	274,533	2,200	170	7.9%	2,962	234	-766	-60 (-25.9%)	-25.9%
Maryland	1,352,964	12,800	2,450	19.1%	14,595	2,787	-1,746	-333 (-12.0%)	-12.0%
Massachusetts	1,418,923	14,900	2,470	16.6%	15,307	2,539	-396	-66 (-2.6%)	-2.6%
Michigan	2,344,068	24,400	4,060	16.7%	25,287	4,211	-931	-155 (-3.7%)	-3.7%
Minnesota	1,284,063	14,100	2,120	15.1%	13,852	2,093	210	32 (1.5%)	1.5%
Mississippi	755,555	9,100	930	10.2%	8,151	832	951	97 (11.7%)	11.7%
Missouri	1,425,436	15,800	1,900	12.0%	15,377	1,845	445	53 (2.9%)	2.9%
Montana	223,563	900	70	8.0%	2,412	192	-1,546	-123 (-64.1%)	-64.1%
Nebraska	459,221	3,800	490	13.1%	4,954	648	-1,179	-154 (-23.8%)	-23.8%

Nevada	665,008	7,200	1,430	19.9%	7,174	1,431	-4	-1 (-0.1%)	-0.1%
New Hampshire	287,234	3,000	330	10.9%	3,099	338	-82	-9 (-2.6%)	-2.6%
New Jersey	2,065,214	17,300	4,160	24.0%	22,278	5,357	-4,997	-1,202 (-22.4%)	-22.4%
New Mexico	518,672	3,000	470	15.4%	5,595	864	-2,548	-394 (-45.5%)	-45.5%
New York	4,324,929	53,600	13,500	25.2%	46,655	11,754	6,945	1,750 (14.9%)	14.9%
North Carolina	2,281,635	24,000	3,100	12.9%	24,613	3,182	-637	-82 (-2.6%)	-2.6%
North Dakota	149,871	1,700	140	8.6%	1,617	139	36	3 (2.2%)	2.2%
Ohio	2,730,751	36,100	6,160	17.1%	29,458	5,036	6,602	1,129 (22.4%)	22.4%
Oklahoma	929,666	8,600	1,150	13.4%	10,029	1,342	-1,410	-189 (-14.1%)	-14.1%
Oregon	866,453	8,500	1,180	13.9%	9,347	1,295	-829	-115 (-8.9%)	-8.9%
Pennsylvania	2,792,155	31,600	6,310	20.0%	30,120	6,011	1,499	299 (5.0%)	5.0%
Rhode Island	223,956	2,700	420	15.7%	2,416	380	263	41 (10.9%)	10.9%
South Carolina	1,080,474	11,400	1,250	11.0%	11,656	1,287	-302	-33 (-2.6%)	-2.6%
South Dakota	202,797	2,100	160	7.6%	2,188	165	-57	-4 (-2.6%)	-2.6%
Tennessee	1,496,001	15,700	2,440	15.5%	16,138	2,503	-418	-65 (-2.6%)	-2.6%
Texas	6,865,824	99,100	14,320	14.4%	74,065	10,701	25,019	3,615 (33.8%)	33.8%
Utah	871,027	8,100	1,670	20.5%	9,396	1,929	-1,254	-258 (-13.3%)	-13.3%
Vermont	129,233	1,300	130	9.8%	1,394	136	-110	-11 (-7.9%)	-7.9%
Virginia	1,853,677	19,400	3,320	17.2%	19,997	3,430	-622	-107 (-3.1%)	-3.1%
Washington	1,581,354	9,600	1,700	17.8%	17,059	3,039	-7,500	-1,336 (-44.0%)	-44.0%
West Virginia	387,418	4,000	580	14.4%	4,179	603	-176	-25 (-4.2%)	-4.2%
Wisconsin	1,339,492	14,700	2,150	14.7%	14,450	2,118	244	36 (1.7%)	1.7%
Wyoming	135,402	1,500	140	9.7%	1,461	141	22	2 (1.5%)	1.5%

Table S4: Comparing results by state

State	State cases	Origin cases	Diff	% Diff	State AC	Origin AC	Diff	% Diff
Montana	866	2,412	-1,546	-64.1%	69	192	-123	-64.1%
Louisiana	5,616	12,061	-6,445	-53.4%	653	1,401	-749	-53.4%
Iowa	4,193	7,853	-3,660	-46.6%	519	971	-453	-46.6%
Illinois	18,264	33,756	-15,492	-45.9%	4,509	8,333	-3,824	-45.9%
New Mexico	3,047	5,595	-2,548	-45.5%	471	864	-394	-45.5%
Washington	9,559	17,059	-7,500	-44.0%	1,703	3,039	-1,336	-44.0%
Georgia	19,165	26,878	-7,713	-28.7%	2,772	3,887	-1,115	-28.7%
Kansas	5,781	7,842	-2,061	-26.3%	787	1,067	-281	-26.3%
Maine	2,196	2,962	-766	-25.9%	173	234	-60	-25.9%
California	75,829	100,270	-24,442	-24.4%	19,205	25,395	-6,190	-24.4%
Nebraska	3,775	4,954	-1,179	-23.8%	494	648	-154	-23.8%
New Jersey	17,281	22,278	-4,997	-22.4%	4,155	5,357	-1,202	-22.4%
Oklahoma	8,619	10,029	-1,410	-14.1%	1,154	1,342	-189	-14.1%
Utah	8,142	9,396	-1,254	-13.3%	1,672	1,929	-258	-13.3%
Maryland	12,849	14,595	-1,746	-12.0%	2,454	2,787	-333	-12.0%
Oregon	8,517	9,347	-829	-8.9%	1,180	1,295	-115	-8.9%
Delaware	2,036	2,220	-184	-8.3%	326	355	-29	-8.3%
Vermont	1,285	1,394	-110	-7.9%	126	136	-11	-7.9%
Connecticut	8,265	8,814	-549	-6.2%	1,502	1,601	-100	-6.2%
West Virginia	4,003	4,179	-176	-4.2%	578	603	-25	-4.2%
Alabama	11,722	12,216	-494	-4.0%	1,381	1,439	-58	-4.0%
Michigan	24,356	25,287	-931	-3.7%	4,056	4,211	-155	-3.7%
Kentucky	10,650	11,040	-389	-3.5%	1,591	1,649	-58	-3.5%
Virginia	19,375	19,997	-622	-3.1%	3,323	3,430	-107	-3.1%
New Hampshire	3,017	3,099	-82	-2.6%	329	338	-9	-2.6%
Arkansas	7,476	7,675	-199	-2.6%	864	887	-23	-2.6%
Massachusetts	14,910	15,307	-396	-2.6%	2,473	2,539	-66	-2.6%

South Carolina	11,354	11,656	-302	-2.6%	1,254	1,287	-33	-2.6%
Tennessee	15,720	16,138	-418	-2.6%	2,438	2,503	-65	-2.6%
South Dakota	2,131	2,188	-57	-2.6%	161	165	-4	-2.6%
Colorado	12,879	13,221	-342	-2.6%	3,009	3,089	-80	-2.6%
North Carolina	23,976	24,613	-637	-2.6%	3,099	3,182	-82	-2.6%
Florida	42,055	43,173	-1,118	-2.6%	5,360	5,502	-142	-2.6%
Nevada	7,170	7,174	-4	-0.1%	1,430	1,431	-1	-0.1%
Wyoming	1,482	1,461	22	1.5%	144	141	2	1.5%
Minnesota	14,061	13,852	210	1.5%	2,124	2,093	32	1.5%
Wisconsin	14,694	14,450	244	1.7%	2,154	2,118	36	1.7%
Idaho	4,724	4,629	96	2.1%	593	581	12	2.1%
North Dakota	1,652	1,617	36	2.2%	142	139	3	2.2%
Missouri	15,821	15,377	445	2.9%	1,898	1,845	53	2.9%
Pennsylvania	31,619	30,120	1,499	5.0%	6,310	6,011	299	5.0%
Rhode Island	2,679	2,416	263	10.9%	422	380	41	10.9%
Mississippi	9,101	8,151	951	11.7%	929	832	97	11.7%
New York	53,600	46,655	6,945	14.9%	13,504	11,754	1,750	14.9%
Ohio	36,060	29,458	6,602	22.4%	6,165	5,036	1,129	22.4%
Indiana	21,263	17,350	3,913	22.6%	3,852	3,143	709	22.6%
Arizona	21,538	17,573	3,965	22.6%	4,623	3,772	851	22.6%
D.C.	1,433	1,088	346	31.8%	386	293	93	31.8%
Texas	99,084	74,065	25,019	33.8%	14,316	10,701	3,615	33.8%

Figure S1: NO2 concentration (ug/m³) by living location

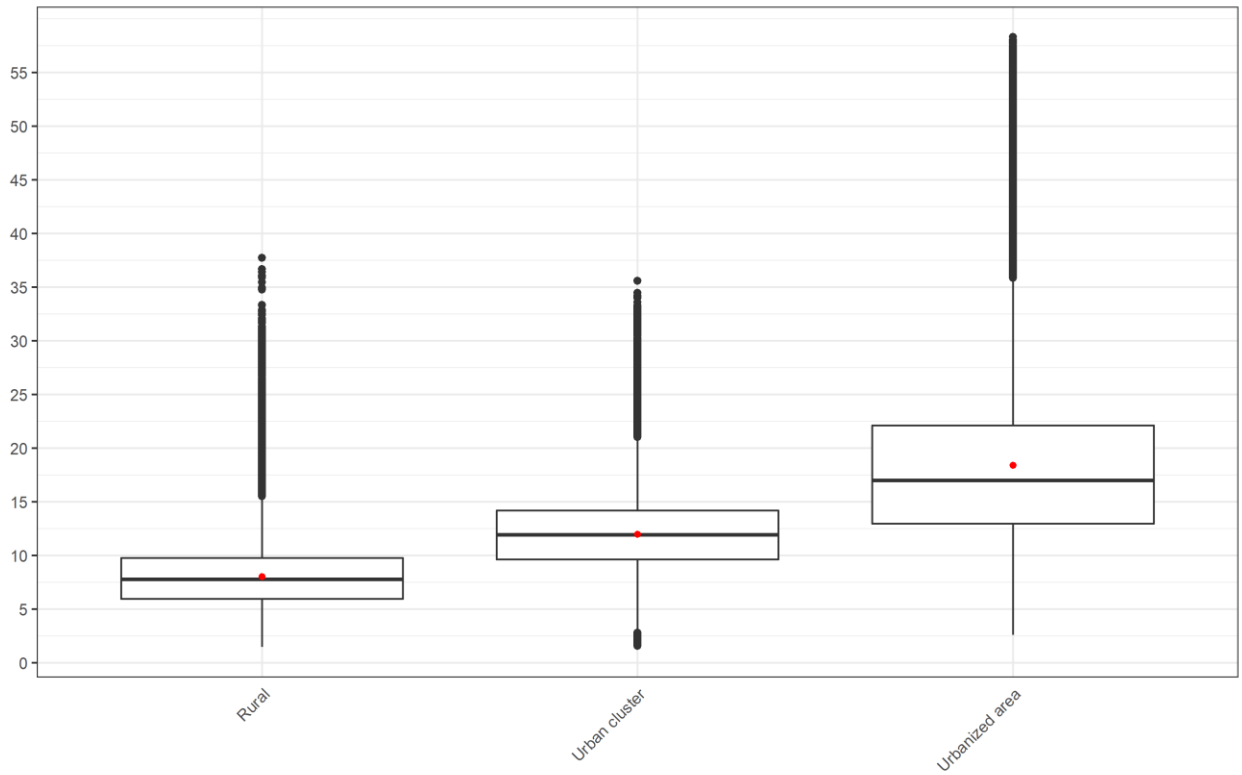

Figure S2: NO2 concentration (ug/m3) by median income group

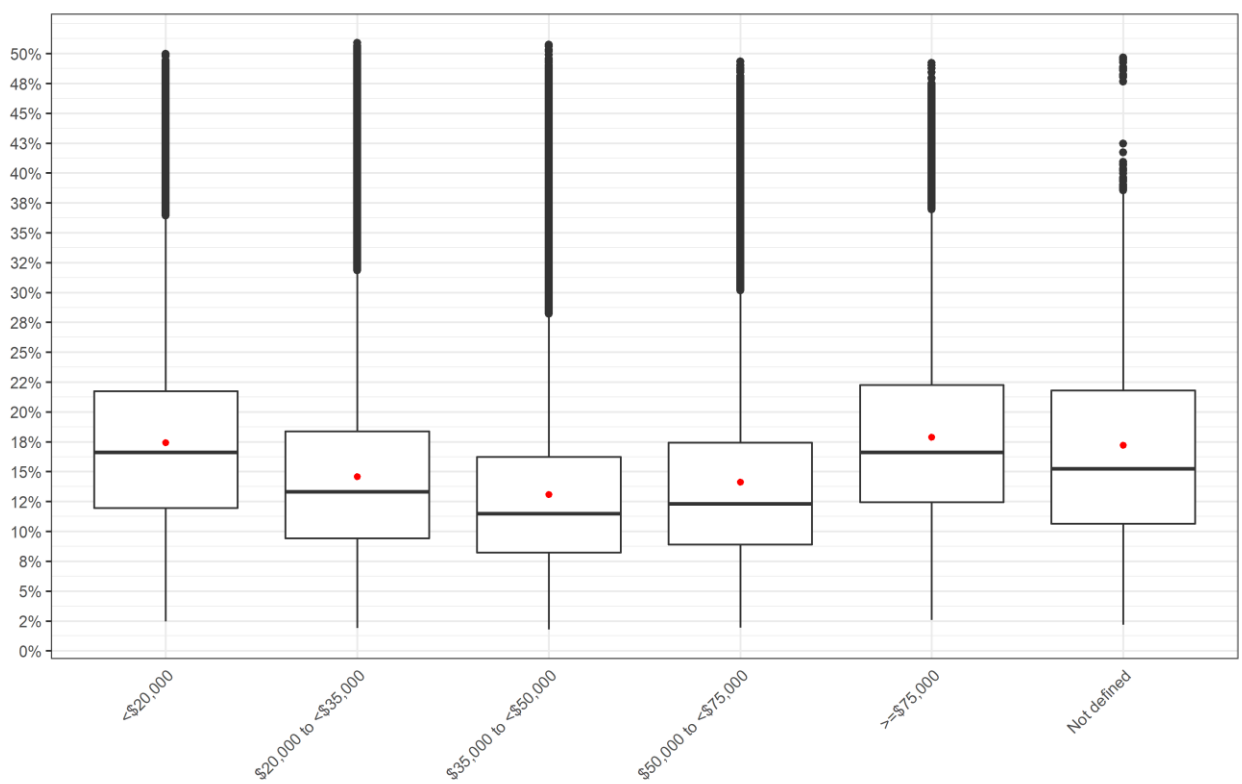

Figure S3: NO2 concentration (ug/m3) by living location stratified into median income group

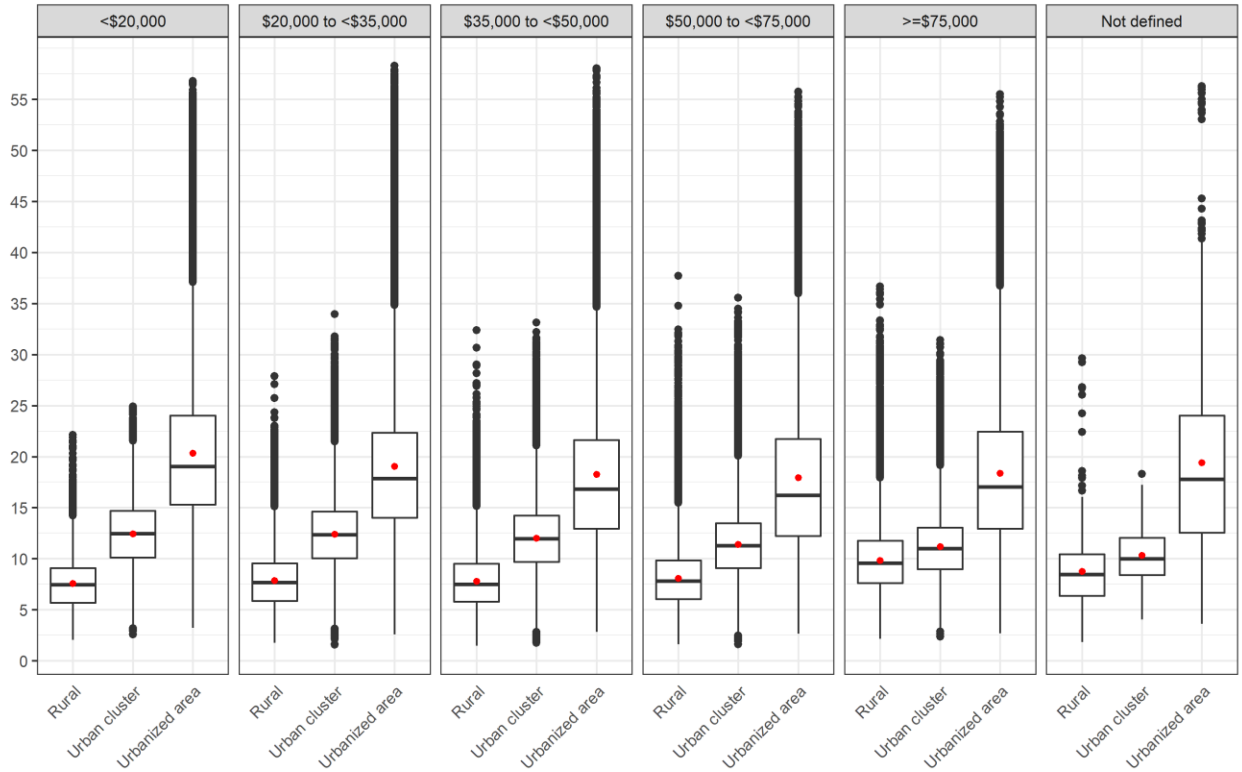

Figure S4: NO2 concentration (ug/m3) by median income group stratified into living location

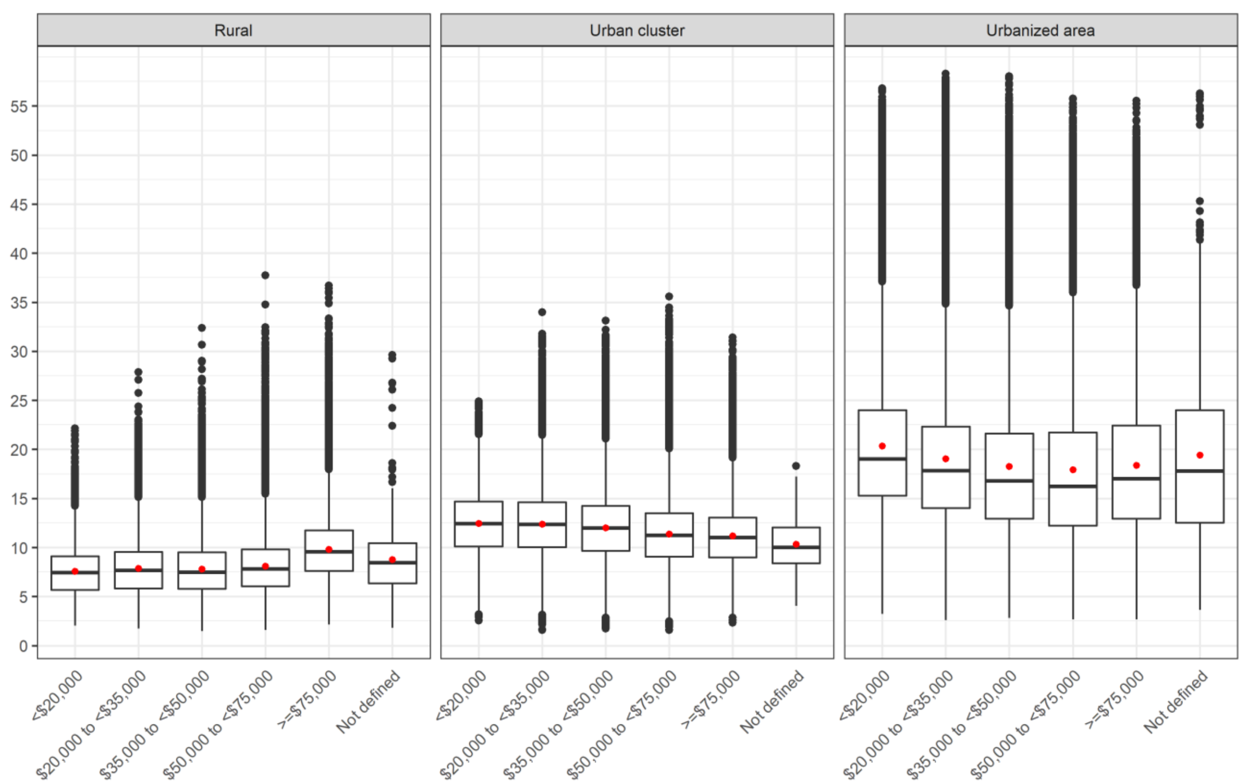

Figure S5: NO2 concentration (ug/m3) by state

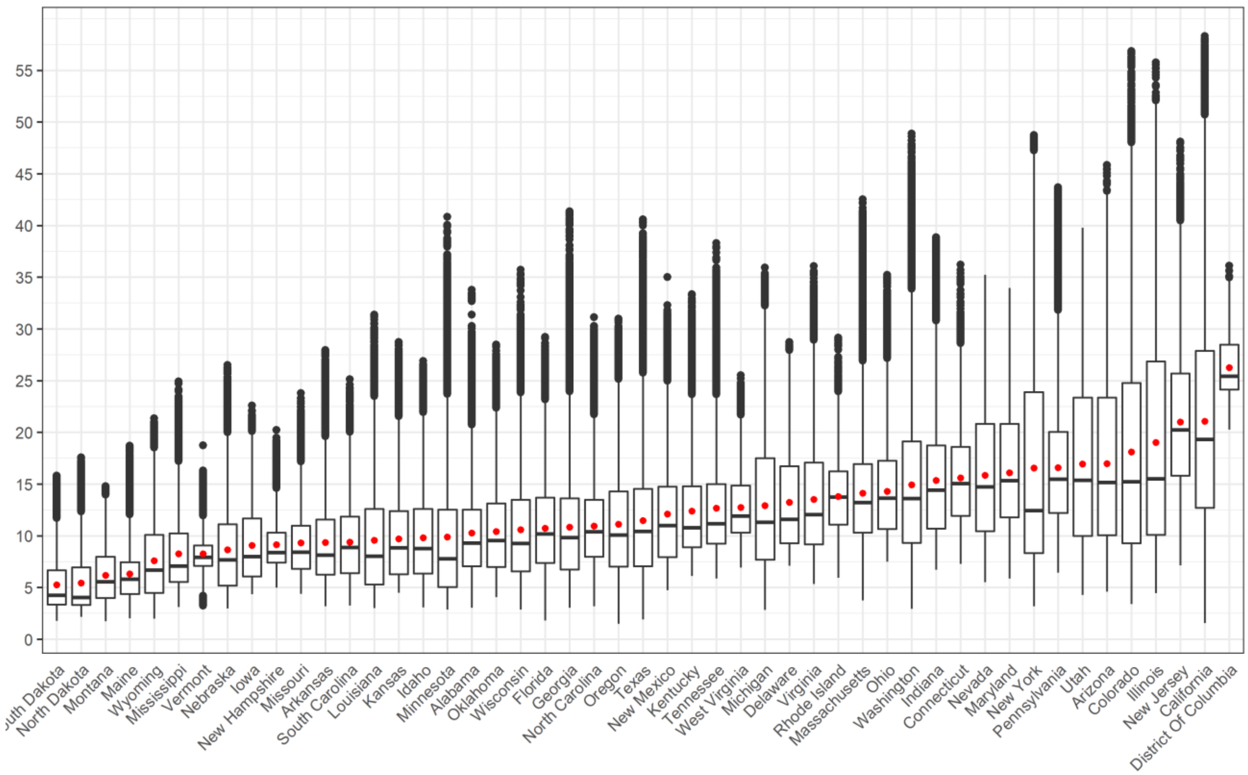

Figure S6: NO2 concentration (ug/m3) by state and median income group

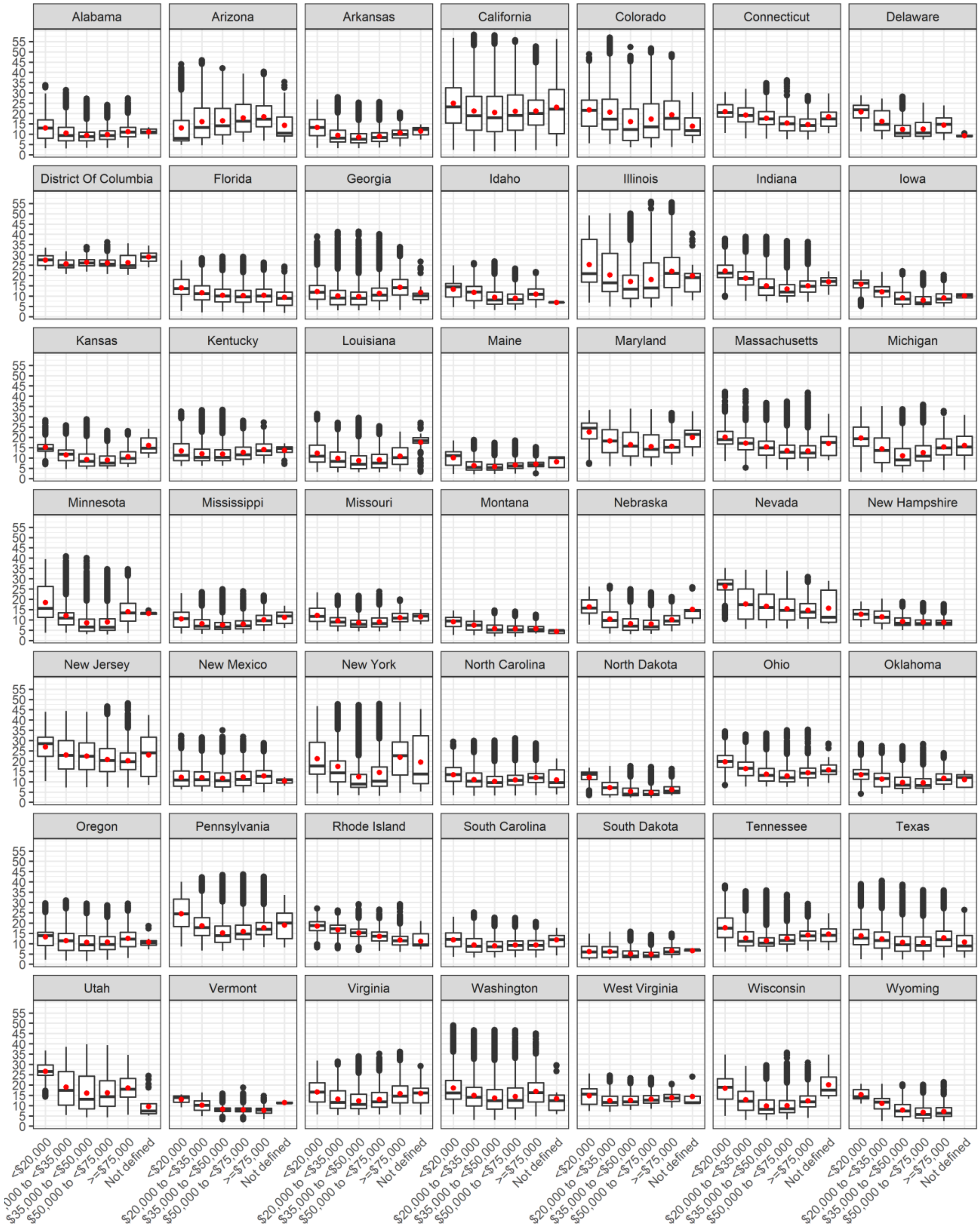

Figure S7: NO2 concentration (ug/m3) by state and living location

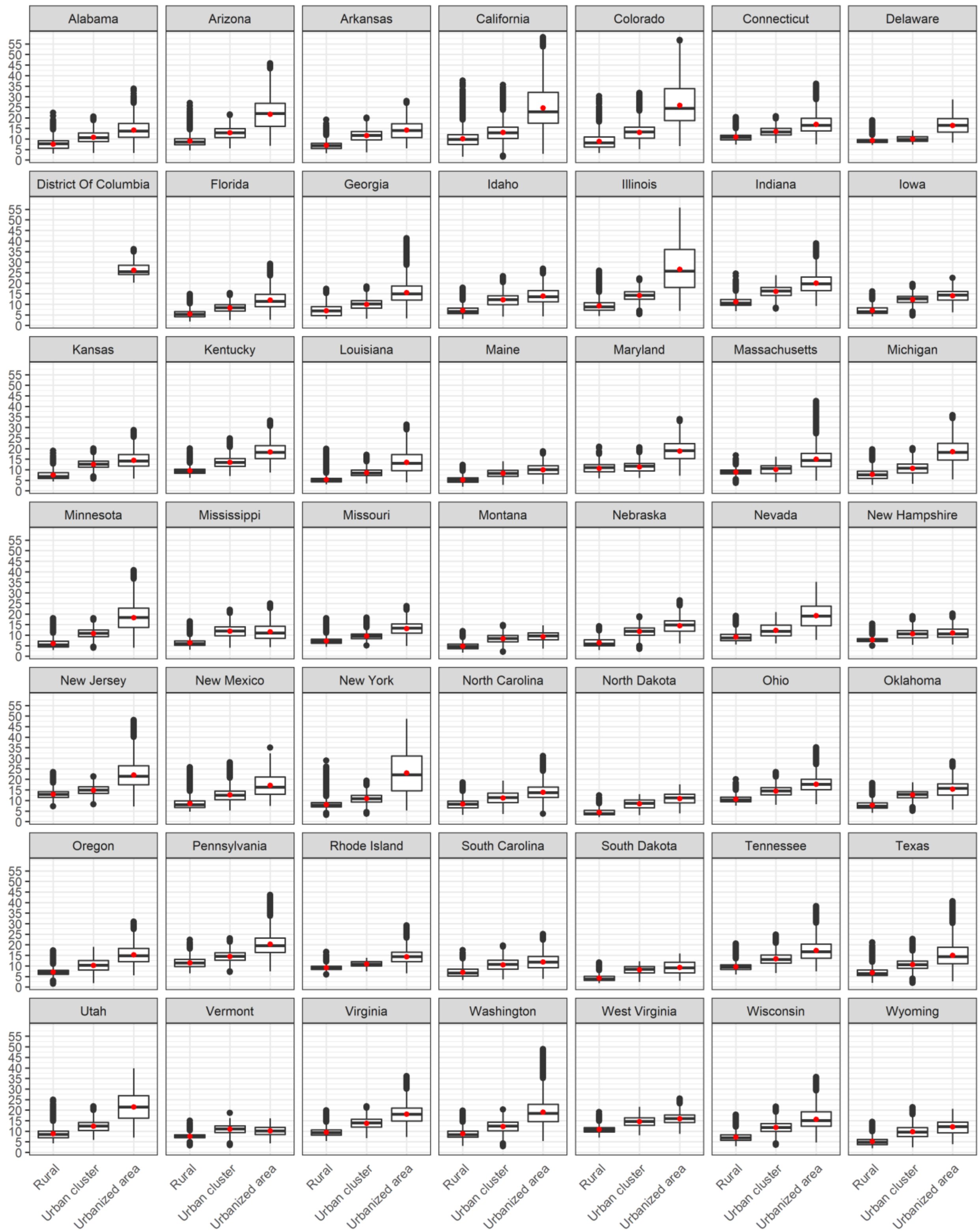

Figure S8: Attributable Fraction by living location

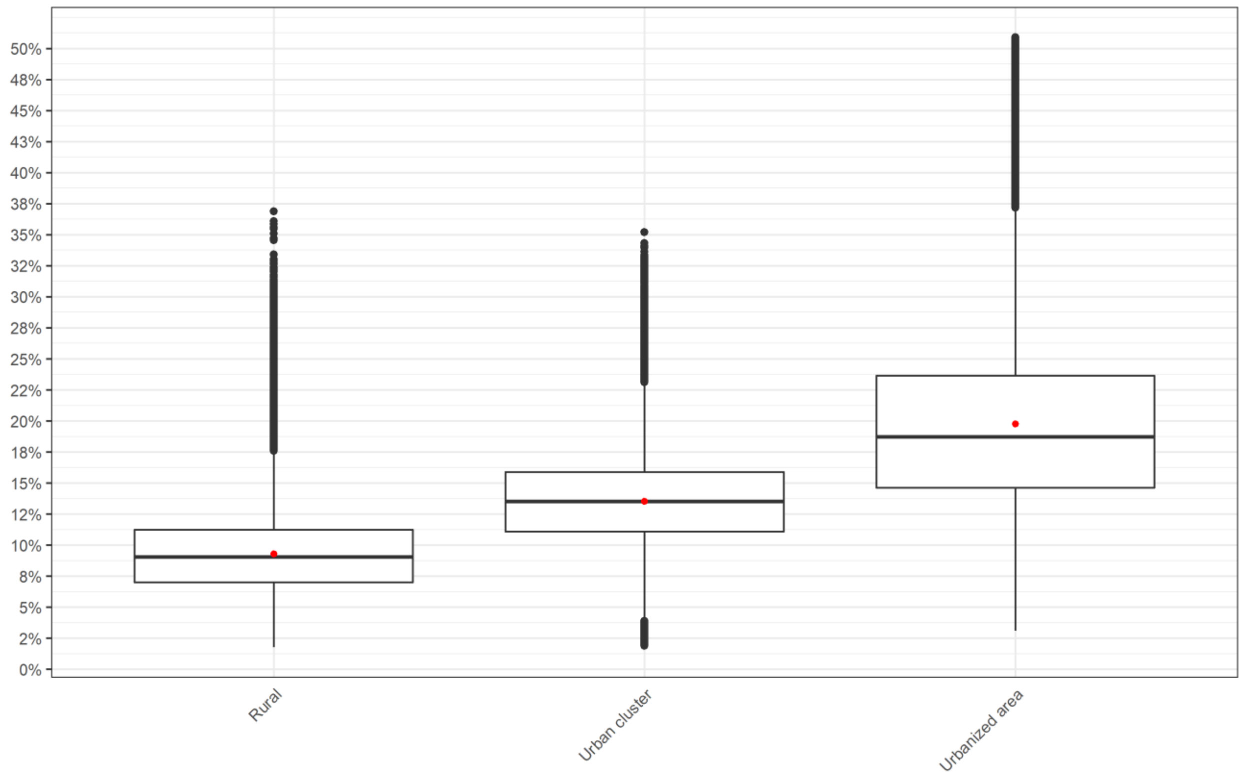

Figure S9: Attributable Fraction by median income group

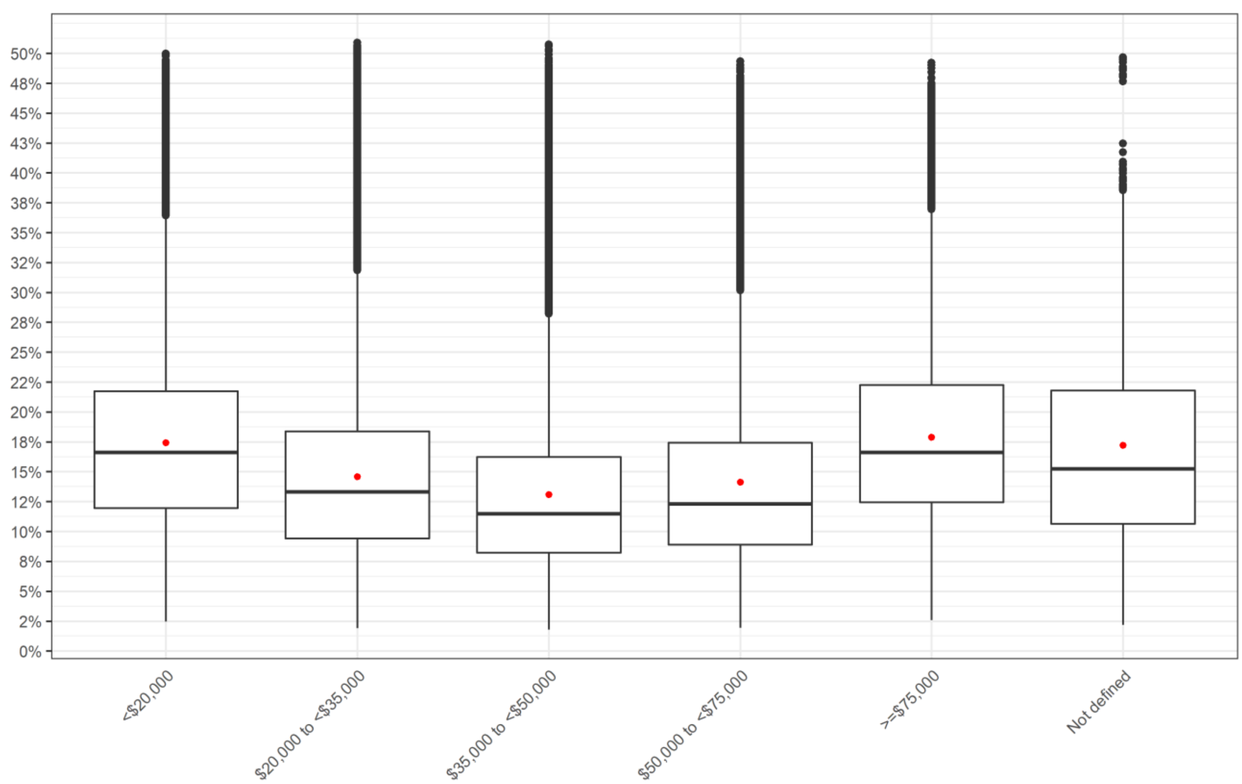

Figure S10: Attributable Fraction by living location stratified into median income group