

# Reported neighborhood traffic and the odds of asthma/asthma like symptoms: a cross-sectional analysis of a multi-racial cohort of children

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## Research

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# Abstract

**Background:** Respiratory symptoms and asthma in children pose a significant clinical and public health burden. Our aim was to examine exposures to environmental air pollution in relation to asthma and related symptoms in a multi-racial cohort of children.

**Methods:** We conducted a cross-sectional analysis evaluating the association between reported neighborhood traffic (a proxy for traffic-related air pollution) and asthma among 855 children aged 4 to 8 years old who participated in the Environmental Influences on Child Health Outcomes (ECHO) cohort. The primary outcome, asthma/asthma like symptoms (defined as current and/or past physician diagnosed asthma, past wheezing, or nighttime cough or wheezing in the past 12 months), was assessed by parental report via questionnaire. The relationship between the primary exposure and asthma/asthma like symptoms was examined using logistic regression.

**Results:** The prevalence of asthma/asthma like symptoms was 23%. Fifteen percent of parents responded “Agree” or “Strongly Agree” to the question, “There is so much traffic along the streets that it makes it difficult or dangerous to walk with my child in my neighborhood” (n=129/855). Children whose parents had affirmed significant neighborhood traffic had a higher odds of having asthma/asthma like symptoms than children without significant neighborhood traffic [adjusted OR=1.78 (95% CI: 1.10, 2.88)] after controlling for child’s race-ethnicity, age, sex, maternal education level, family history of asthma, presence of play equipment in the home environment, public parks in the neighborhood and obesity. Other factors significantly associated with asthma/asthma like symptoms were: non-Hispanic Black and Hispanic race/ethnicity [OR=2.53 (95% CI: 1.43, 4.50)] and [OR=2.25 (95% CI: 1.28, 3.94), respectively, vs. non-Hispanic White referent], play equipment in the home environment or backyard [OR=1.60 (95% CI: 1.09, 2.35)], obese status [OR=2.54 (95% CI: 1.55, 4.17)], male sex [OR=1.53 (1.06, 2.22)] and family history of asthma [OR=3.19 (2.20, 4.64)].

**Conclusions:** Reported neighborhood traffic, non-Hispanic Black and Hispanic race/ethnicity, male sex, play equipment within the home environment, obesity, and family history of asthma were associated with greater odds for asthma/asthma like symptoms. Further characterization of neighborhood traffic patterns is needed, since many children live near this source of environmental air pollution and significant racial/ethnic disparities exist.

## Introduction

Asthma is a common chronic disease with varying clinical and biological characteristics.<sup>1–3</sup> The disease is associated with increased morbidity, mortality, increased health care costs and parental work and children’s school absence.<sup>4, 5</sup> In the United States, asthma affects approximately 9.3% of children and this translates to a large clinical and economic burden on the country’s healthcare system.<sup>6–8 9</sup> A recent study reported that asthma-related costs were approximately \$80 billion in 2013 when factors such as missed school/work days, medical costs and mortality were combined.<sup>10</sup>

The interplay between environmental and genetic factors adds to the complexity of asthma. Exposure to environmental factors, such as air pollution, may increase the prevalence of asthma and other adverse respiratory symptoms.<sup>11-13 14-16</sup> Emerging evidence also shows that residential proximity to a major roadway and exposure to traffic-related air pollution (TRAP) during childhood is associated with the onset of asthma<sup>17-19</sup> as well as acute airway inflammation in individuals with and without asthma.<sup>20-25</sup>

There is mounting evidence that living near heavy traffic is associated with increased rates of asthma, cardiovascular disease, and dementia.<sup>26-30</sup> Additionally, air pollution exposure gradients at small scales such as neighborhoods are associated with adverse health effects.<sup>31, 32</sup> Although direct assessment of individual TRAP exposure is ideal, it presents a myriad of logistical challenges in population-based studies. Simple proxies, such as distance to roadways and traffic estimates or counts, can also be used to assign individual TRAP exposure.<sup>26, 32-41</sup>

Economically disadvantaged and minority populations share a disproportionate burden of air pollution exposure and risk.<sup>42</sup> Growing evidence shows that these populations experience higher residential exposure to traffic and TRAP than non-minorities and persons of higher socioeconomic status.<sup>43, 44</sup> Children, are more susceptible to air pollution exposures than adults due to immature immune systems, developing lungs, higher breathing rates, a greater extent of mouth breathing and more outdoor activities.<sup>12, 45, 46</sup>

Racially diverse cohort studies can provide further evidence and advance the state of the science on the relationships between asthma and air pollution. A recent international workshop highlighted the need to clarify modes of asthma progression and exacerbations during pre-puberty and the relevance of environmental exposures.<sup>47</sup> With the presence of a 'triple jeopardy', namely the combination of impaired respiratory health, racial/ethnic status, and TRAP exposures, it is essential to identify subgroups of the population that may need to be targeted for intervention. Accordingly, we used parent-reported density of neighborhood traffic as a proxy measure for TRAP and evaluated its association with the prevalence of reported asthma/asthma like symptoms in children 4 to 8 years old, who participated in the Environmental Influences on Child Health Outcomes (ECHO) cohort (n = 855). In this racially and geographically diverse cohort we sought to determine what proportion of children were reported to have high neighborhood traffic and whether this exposure was associated with asthma/asthma like symptoms.

## Methods

### Study population

This study leveraged a unique resource from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Fetal Growth Studies (NICHD FGS). Specifically, a cohort of racially, ethnically and geographically diverse healthy women and fetuses were studied longitudinally across twelve sites in

the United States during pregnancy from July 2009 to January 2013, to characterize optimal fetal growth velocity.<sup>48</sup>

The ECHO study was designed and implemented to follow up with the NICHD FGS cohort. There were 1116 mother singleton child pairs recruited from May 2017 through April 2019 for ECHO. Ten of the original twelve NICHD FGS study sites participated in ECHO: Christiana Care Health System (DE), Columbia University Irving Medical Center (NY), Fountain Valley Regional Hospital and Medical Center (CA), Medical University of South Carolina (SC), Miller Children's Hospital Long Beach Memorial Medical Center (CA), New York Hospital Queens (NY), Northwestern University Feinberg School of Medicine (IL), St. Peter's University Hospital (NJ), University of Alabama at Birmingham (AL), and University of California at Irvine (CA).

Mothers were invited to participate in self-report surveys while physical and neurodevelopmental data were collected from children. If a mother-child pair was unable or unwilling to attend an in-person visit, they could still participate in a home visit, telephone visit or a short computer survey. Participants were remunerated for their time, depending on the type of visit completed. Written informed consent was obtained from the parent or legal guardian of each enrolled child and depending on child age and state regulations child assent was obtained when required. We used Research Electronic Data Capture (REDCap) to enter data from paper forms as needed, to allow electronic form data to be directly captured, and to securely store data.

## **Questionnaires**

Validated questionnaires included the Preschool-age Children's Physical Activity Questionnaire (Pre-PAQ)<sup>49</sup> and the International Study of Asthma and Allergies in Childhood (ISAAC)<sup>50</sup> questionnaire. Detailed questions were asked on child and family history of disease including asthma/asthma like symptoms as well as questions related to demographic characteristics. The adult participant (99% were the mother) filled out these surveys either at home or during a study visit, with site personnel acting as translators as needed.

## **Exposure variables**

**Primary Exposures:** Reported current exposure to neighborhood traffic defined by the question, "There is so much traffic along the streets that it makes it difficult or dangerous to walk with my child in my neighborhood." This statement is from a set of eight found in the Pre-PAQ (Q22). Children were considered exposed to significant neighborhood traffic when their mothers responded "Agree" or "Strongly Agree" to the above question. Accordingly, when mothers responded "Disagree" or "Strongly disagree", those children were considered unexposed to significant neighborhood traffic.

**Secondary Exposures:** We included maternal response to questions on the home environment and neighborhood to assess other environmental factors that could influence a child's exposure to TRAP. First, we examined the remaining seven questions in the Pre-PAQ (Q22) on neighborhood, with the same four

Likert scale responses as above: i) safety when playing outdoors; ii) presence of local footpaths; iii) barriers or dangers to walking; iv) sufficient traffic lights or pedestrian crossings; v) unsafe levels of crime; vi) shops within walking distance; and vii) dangers in local parks. Then, for the home environment we looked at access to any of the following facilities within the backyard or home environment (Pre-PAQ Q18): i) Play equipment (e.g. swing set, slide, climbing gym); ii) Pool or spa; and iii) area suitable to ride a tricycle or scooter. Thirdly, for additional neighborhood characteristics, we evaluated maternal response to questions on whether a child's local neighborhood had the following places or facilities where he/she can play and be physically active (Pre-PAQ Q21): i) Open areas such as beaches, rivers, natural reserves; ii) Public park or oval; iii) Playground; iv) Public swimming pool; v) Gym that offers programs for young children (e.g. kindergym, playgym etc.); and vi) Club that offers activities/sports for young children (e.g. soccer, dance etc.).

### **Outcome variable**

The presence of wheezing, cough, and/or asthma was assessed by parental report using the validated ISAAC questionnaire.<sup>51</sup> Asthma was considered positive when mothers responded "yes" to the question: "Has a doctor or other health care provider ever told you that your child has or had the following condition: Asthma?". Wheezing/cough symptoms were considered positive when mothers responded "yes" to any of the following questions: Q1: "Has a doctor or other health care provider ever told you that your child has or had the following conditions: Wheezing or whistling in the chest?"; Q2: "In the past 12 months, has your child's chest sounded wheezy during or after exercise?"; Q3: "In the past 12 months, has your child had a dry cough at night, apart from a cough associated with a cold or chest infection?". In this analysis, we combine asthma, cough, and/or wheezing symptoms as *one primary outcome* termed: asthma/asthma like symptoms (Outcome 3 in Figure 1).

### **Covariates**

For adjusted analyses, we include the following the covariates into the model, as these have been identified as potential confounders in the literature: 1) child's sex, 2) child's race-ethnic group, 3) positive family history of asthma (asthma diagnosed in parents, siblings and/or grandparents), 4) maternal education level (less than or up to high school or greater than high school, 5) obese status of child, defined as having a BMI-for-age  $\geq 95^{\text{th}}$  %ile.<sup>52, 53</sup> Further, we looked at other covariates such as presence of cats or dogs during child's first year and/or within the past 12 months, secondhand/environmental tobacco smoke exposure, as well as responses to 16 questions from the Pre-PAQ (these described the home and neighborhood characteristics, such as the presence of parks, pools, shops, street safety, etc.).

### **Statistical analysis**

The primary aims of the study were to determine what proportion of children had high neighborhood traffic and whether this exposure was associated with asthma/asthma like symptoms. We examined differences in children with or without asthma/asthma like symptoms (and with or without significant

neighborhood traffic) using  $\chi^2$  tests for categorical variables and two-sample t-tests for continuous variables.

Next, we conducted a series of logistic regressions to evaluate the association between reported neighborhood traffic exposure and the occurrence of any reported asthma/asthma like symptoms in the cohort. Model 1 included neighborhood traffic as the primary variable, and demographics as covariates. Models 2 and 3 incorporated additional covariates related to outdoor air exposure found to be significantly related to asthma/asthma like symptoms. Model 4 included all statistically significant covariates and added child's obesity status to determine whether the latter affected the model.

We also examined the impact of including adjustment for factors such as mode of delivery (vaginal or caesarian section), child's use of antibiotic medication in the past year, child's stay at the neonatal intensive care unit after birth and gestational age at delivery. Lastly, we stratified the analysis by sex.

To check the robustness of our results, we conducted a sensitivity analysis by limiting the primary health outcome to current asthma and/or current asthma like symptoms as opposed to current or past asthma/asthma like symptoms. We report result in terms of p-values, adjusted odds ratios (OR) and 95% confidence intervals. All statistical tests were two-tailed, and  $p \leq 0.05$  was considered statistically significant. Analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). The odds ratios plot was derived using 'ggplot2' function in R.<sup>54</sup>

## Results

For this study, 1116 children aged 4 to 8 years, born while their mothers participated in the NICHD-FGS study, were enrolled with their mothers in ECHO. Mothers of 879 children completed the study's Child Early Life Questionnaire. However, 2.7% (n=24) were excluded from the statistical analysis due to a lack of response to the question on neighborhood traffic (Figure 2). Hence, the current analysis includes 855 children. The sociodemographic and neighborhood characteristics of participants according to maternal report is provided for the exposure and outcome variables of interest – neighborhood traffic (Table 1) and asthma/asthma like symptoms (Table 2), respectively. The prevalence of maternal report of doctor-diagnosed asthma was 13%; wheezing symptomsighttime cough was 19%; and asthma and/or wheezing was 23% (hereafter asthma/asthma like symptoms) (Table 1).

### Differences by race-ethnic group

Children of Hispanic (34.9%) and non-Hispanic Black (39.5%) race/ethnicity were more likely to be exposed to significant neighborhood traffic than non-Hispanic White children (12.4%) ( $p$ -value < 0.0001) (Table 1). Overall, mothers reported that 15.1% (n=129) of the children in this analysis were exposed to significant neighborhood traffic (Table 2). Hispanic (31.5%) and non-Hispanic Black (40.1%) children were more likely to report asthma/asthma like symptoms than non-Hispanic or Asian children ( $p$ -value < 0.0001) (Table 2).

## **Bivariate analysis – neighborhood traffic**

Children exposed to neighborhood traffic were similar in terms of male sex, age, family history of asthma, obese status, presence of cats or dogs during child's first year and/or within the past 12 months ( $p>0.1$ ) when compared to those unexposed to neighborhood traffic (Table 1). Walking distance to local shops, having a pool or spa in the backyard and access to public swimming pool were also not significantly different among the two neighborhood traffic groups. Maternal education, race, asthma, and wheezing symptoms as well as responses to a majority of the neighborhood factors (13/16 questions from the Pre-PAQ) differed significantly depending on reported neighborhood traffic ( $p<0.05$ , Table 1). Secondhand smoke exposure showed marginal significance with increased neighborhood traffic ( $p=0.08$ ), and children with any household pet (dog and/or cat) were less likely to be exposed to neighborhood traffic ( $p=0.02$ ) but after adjusting for demographics and family history of asthma this was no longer any statistical significance.

## **Bivariate analysis – asthma/asthma like symptoms**

As shown in Table 2, the following factors were more likely to occur among children with asthma/asthma like symptoms than in those without such symptoms: Male sex (56.9% vs 49.5%,  $p=0.07$ ), non-Hispanic Black (40.1% vs 26.6%) or Hispanic (31.5% vs 24.2%) [ $p<0.0001$ ], family history of asthma (55.8% vs 26.8%,  $p<0.0001$ ), obese status, (21.3% vs 8.2%,  $p<0.001$ ), child's exposure to second hand smoke (15.7% vs 9.6%,  $p=0.02$ ), neighborhood traffic (21.8% vs 13.1%,  $p=0.003$ ), dangers in the local parks (e.g., unleashed dogs or undesirable people) [13.2% vs 8.2%,  $p=0.04$ ], and the presence of a public park or oval in the local neighborhood for the child to play and be physically active (90.4% vs 86.0%,  $p=0.03$ ). On the other hand, having usable footpaths on most of the streets in local area (72.6% vs 79.6%,  $p=0.04$ ) and sufficient traffic lights or pedestrian crossings to make it safe to walk around neighborhood (71.6% vs 78.9%,  $p=0.06$ ) were reported less frequently by mothers of children with asthma/asthma like symptoms than in those without such symptoms.

Table 1. Comparison of the Environmental Influences on Child Health Outcomes Fetal Growth Study (ECHO-FGS) cohort by reported neighborhood traffic exposure. P values in bold indicate statistical significance (P<0.05)

Variable	All children in current study (n=855) %	Exposed to Neighborhood Traffic (n=129) %	Unexposed to Neighborhood Traffic (n=726) %	p-value for $\chi^2$ or t test
Child age in years, mean (SD)	6.9 (1.0)	6.7 (0.9)	6.9 (1.0)	0.09
Physician diagnosed asthma only (Asthma) (current or past)	13.9%	20.2%	12.8%	<b>0.03</b>
Wheezing or respiratory symptoms only (current or past)	19.1%	25.6%	17.9%	<b>0.04</b>
Primary Outcome: Asthma/asthma like symptoms (current or past)	23.0%	33.3%	21.2%	<b>0.003</b>
Male child	51.2%	55.0%	50.6%	0.3
Race of child				
Non-Hispanic White (NHW)	31.1%	12.4%	34.4%	<b>&lt;.0001</b>
Non-Hispanic Black (NHB)	29.7%	39.5%	28.0%	
Hispanic	25.9%	34.9%	24.2%	
Asian	13.1%	13.2%	13.1%	
Mother Education				
Less than or up to high school	21.6%	34.9%	19.3%	<b>&lt;.0001</b>
More than high school	78.4%	65.1%	80.7%	
Family history of asthma	33.5%	34.9%	33.2%	0.9
Child's BMI for age percentile				
Obese (BMI for age percentile $\geq$ 95)	11.2%	15.5%	10.5%	0.2
Child exposed to any second hand smoke	11.0%	15.5%	10.2%	0.08
Household pets				
Cat at home during child's first year and/or in the past 12 months	18.6%	16.3%	19.0%	0.5
Dog at home during child's first year and/or in the past 12 months	44.7%	40.3%	45.5%	0.3
Pets (dog and/or cat) at home during child's first year and/or in the past 12 months	52.8%	43.4%	54.4%	<b>0.02</b>
Preschool-aged Children's Physical Activity Questionnaire (Pre-PAQ) Q22 Variables [strongly agree or agree]				
Safety: <i>It is safe for my child to play outdoors in my neighborhood (if supervised).</i>	93.7%	79.1%	96.3%	<b>&lt;.0001</b>
Footpaths: <i>There are usable footpaths on most of the streets in my local area.</i>	78.0%	51.9%	82.6%	<b>&lt;.0001</b>
Walk: <i>There are major barriers or dangers to walking with my child in my neighborhood that make it hard to get from place to place (e.g., major roads, railway lines, canals, storm water drains or rivers).</i>	11.9%	45.7%	5.9%	<b>&lt;.0001</b>
Sufficient light: <i>There are sufficient traffic lights or pedestrian crossings to make it safe to walk with my child around my neighborhood.</i>	77.2%	48.8%	82.2%	<b>&lt;.0001</b>
Crime: <i>The level of crime in my neighborhood makes it unsafe to go on walks with my child during the day.</i>	9.5%	31.8%	5.5%	<b>&lt;.0001</b>
Shops: <i>The local shop(s) are within easy walking distance of my home.</i>	54.9%	54.3%	55.0%	1.0
Danger: <i>There are dangers (e.g., dogs or undesirable people) in the local park(s) so I avoid taking my child there.</i>	9.4%	32.6%	5.2%	<b>&lt;.0001</b>
Preschool-aged Children's Physical Activity Questionnaire (Pre-PAQ) Q18 (please tick as many responses as apply) [Yes]				
Do you have access to any of the following facilities within your backyard or home environment?				
Play equipment (e.g., swing set, slide, climbing gym)	45.7%	31.8%	48.2%	<b>0.0006</b>
Pool or spa	19.8%	19.4%	19.8%	0.9
Area suitable to ride a tricycle, bike or scooter etc.	78.0%	60.5%	81.1%	<b>&lt;.0001</b>
Preschool-aged Children's Physical Activity Questionnaire (Pre-PAQ) Q21 Variables [Yes]				
Does your local neighbourhood have the following places or facilities where your child can be play and be physically active? (please tick as many responses as apply)				
Open areas such as beaches, rivers, natural reserves	41.4%	29.5%	43.5%	<b>0.009</b>
Public park or oval	87.0%	76.7%	88.8%	<b>0.0002</b>
Playground	88.3%	79.1%	89.9%	<b>0.0003</b>
Public swimming pool	52.4%	44.2%	53.9%	0.1
Gym that offers programs for young children e.g. kindergym, playgym etc.	47.6%	35.7%	49.7%	<b>0.008</b>

**Table 2. Comparison of the Environmental Influences on Child Health Outcomes Fetal Growth Study (ECHO-FGS) cohort by primary outcome: asthma/asthma like symptoms. P values in bold indicate statistical significance (P<0.05)**

Variable	Asthma/asthma like symptoms (n=197) %	No asthma/asthma like symptoms (n=658) %	p-value for $\chi^2$ or t test
Child age in years, mean (SD)	6.9 (1.0)	6.8 (1.0)	0.7
Male child	56.9%	49.5%	0.07
Race of child			
NonHispanic White (NHW)	19.3%	34.7%	<b>&lt;.0001</b>
NonHispanic Black (NHB)	40.1%	26.6%	
Hispanic	31.5%	24.2%	
Asian	8.6%	14.4%	
Mother Education			
Less than or up to high school	25.9%	20.4%	0.1
More than high school	74.1%	79.6%	
Family history of asthma	55.8%	26.8%	<b>&lt;.0001</b>
Child's BMI for age percentile			
Obese (BMI for age percentile $\geq 95$ )	21.3%	8.2%	<b>&lt;.0001</b>
Child exposed to any second hand smoke	15.7%	9.6%	<b>0.02</b>
Household pets			
Cat at home during child's first year and/or in the past 12 months	17.3%	19.0%	0.6
Dog at home during child's first year and/or in the past 12 months	45.2%	44.5%	0.9
Pets (dog and/or cat) at home during child's first year and/or in the past 12 months	51.8%	53.0%	0.8
Preschool-aged Children's Physical Activity Questionnaire (Pre-PAQ) Q22 Variables [strongly agree or agree]			
Safety: It is safe for my child to play outdoors in my neighborhood (if supervised).	91.9%	94.2%	0.3
Footpaths: There are usable footpaths on most of the streets in my local area.	72.6%	79.6%	<b>0.04</b>
Walk: There are major barriers or dangers to walking with my child in my neighborhood that make it hard to get from place to place (e.g., major roads, railway lines, canals, storm water drains or rivers).	12.2%	11.9%	0.8
Neighborhood traffic: There is so much traffic along the streets that it makes it difficult or dangerous to walk with my child in my neighborhood.	21.8%	13.1%	<b>0.003</b>
Sufficient light: There are sufficient traffic lights or pedestrian crossings to make it safe to walk with my child around my neighborhood.	71.6%	78.9%	0.06
Crime: The level of crime in my neighborhood makes it unsafe to go on walks with my child during the day.	11.7%	8.8%	0.2
Shops: The local shop(s) are within easy walking distance of my home.	56.9%	54.3%	0.6
Danger: There are dangers (e.g., dogs or undesirable people) in the local park(s) so I avoid taking my child	13.2%	8.2%	<b>0.04</b>
Preschool-aged Children's Physical Activity Questionnaire (Pre-PAQ) Q18 (please tick as many responses as apply) [ Yes]			
Do you have access to any of the following facilities within your backyard or home environment?			
Play equipment (e.g., swing set, slide, climbing gym)	48.7%	44.8%	0.3
Pool or spa	21.8%	19.2%	0.5
Area suitable to ride a tricycle, bike or scooter etc.	77.2%	78.3%	0.9
Preschool-aged Children's Physical Activity Questionnaire (Pre-PAQ) Q21 Variables [Yes]			
Does your local neighbourhood have the following places or facilities where your child can be play and be physically active? (please tick as many responses as apply)			
Open areas such as beaches, rivers, natural reserves	40.1%	41.8%	0.7
Public park or oval	90.4%	86.0%	<b>0.03</b>
Playground	86.3%	88.9%	0.6
Public swimming pool	53.8%	52.0%	0.5
Gym that offers programs for young children e.g. kindergym, playgym etc.	48.7%	47.3%	0.4
Club that offers activities/sports for young children e.g. soccer, dance etc.	58.9%	59.1%	0.4

## Multiple logistic regression models

In demographic adjusted logistic regression models (i.e. models 1-3), neighborhood traffic, the presence of play equipment in the home environment or backyard, and the presence of a public park or oval in the neighborhood were positively associated with asthma/asthma like symptoms (Figure 3). There were positive associations between asthma/asthma like symptoms and the following groups: 1) males, 2) Non-Hispanic blacks, 3) Hispanics, and 4) those with a family history of asthma (Table 3).

The final model in Table 3 (model 4, n=738) revealed that children exposed to significant neighborhood traffic had higher odds of having asthma/asthma like symptoms than children exposed to less neighborhood traffic [OR=1.78 (95% CI: 1.10, 2.88)]. Obese children and children with play equipment in the home environment or backyard had higher odds of having asthma/asthma like symptoms than those without: [OR=1.60 (95% CI: 1.09, 2.35)] and [OR=2.54 (95% CI: 1.55, 4.17)], respectively. Adding obesity status to the model resulted in the presence of a public park becoming non-significant. Non-Hispanic Black and Hispanic children had higher odds of having asthma/asthma like symptoms than non-Hispanic White children: [OR=2.53 (95% CI: 1.43, 4.50)] and [OR=2.25 (95% CI: 1.28, 3.94)] respectively.

Additionally, male children had higher odds of asthma/asthma like symptoms [OR=1.53 (95% CI: 1.06, 2.22)] (Table 3), as did children with a family history of asthma [OR=3.19 (95% CI: 2.20, 4.64)].

**Table 3. Odds ratios with 95% confidence limits for the primary outcome: asthma/asthma like symptoms in relationship to demographics, home and neighborhood characteristics of the Environmental Influences on Child Health Outcomes Fetal Growth Study (ECHO-FGS) cohort.**

	Model 1 (n=835)	Model 2 (n=825)	Model 3 (n=817)	Model 4 (n=738)
Male child	<b>1.52 (1.08, 2.15)</b>	<b>1.57 (1.11, 2.23)</b>	<b>1.54 (1.08, 2.19)</b>	<b>1.53 (1.06, 2.22)</b>
Age of child	1.20 (0.98, 1.46)	1.20 (0.99, 1.47)	1.21 (0.99, 1.47)	1.18 (0.95, 1.45)
Race-Ethnic of child				
NHW	1.00	1.00	1.00	1.00
NHB	<b>2.55 (1.52, 4.29)</b>	<b>2.74 (1.61, 4.67)</b>	<b>2.68 (1.56, 4.59)</b>	<b>2.53 (1.43, 4.50)</b>
Hispanic	<b>2.39 (1.44, 3.98)</b>	<b>2.62 (1.55, 4.42)</b>	<b>2.56 (1.52, 4.34)</b>	<b>2.25 (1.28, 3.94)</b>
Asian	1.41 (0.71, 2.80)	1.58 (0.79, 3.18)	1.50 (0.74, 3.01)	1.40 (0.66, 2.99)
Mother Education	0.93 (0.61, 1.41)	0.91 (0.59, 1.39)	0.97 (0.63, 1.50)	1.08 (0.69, 1.70)
Family History of asthma	<b>3.32 (2.34, 4.70)</b>	<b>3.38 (2.38, 4.81)</b>	<b>3.24 (2.27, 4.63)</b>	<b>3.19 (2.20, 4.64)</b>
Neighborhood Traffic	<b>1.59 (1.02, 2.48)</b>	<b>1.77 (1.13, 2.77)</b>	<b>1.93 (1.22, 3.06)</b>	<b>1.78 (1.10, 2.88)</b>
Play Equipment	---	<b>1.53 (1.07, 2.19)</b>	<b>1.44 (1.00, 2.07)</b>	<b>1.60 (1.09, 2.35)</b>
Public Park	---	---	<b>2.02 (1.07, 3.79)</b>	1.86 (0.98, 3.54)
Obese	---	---	---	<b>2.54 (1.55, 4.17)</b>

### Sensitivity analysis

When we limited the primary health outcome to current asthma and/or current wheezing (19%) as opposed to current or past asthma/asthma like symptoms (23%) the results were similar. The only difference was that play equipment in the backyard was no longer statistically significant [OR=1.42 (95% CI: 0.95, 2.14)]. As before, mother's education [OR=1.07 (95% CI: 0.67, 1.71)], Asian race [OR=1.38 (95% CI: 0.58, 3.25)] and the presence of neighborhood parks [OR=1.83 (95% CI: 0.92, 3.62)] did not reach statistical significance. All other variables remained statistically significant: Male [OR=1.61 (95% CI: 1.09, 2.40)]; non-Hispanic Black [OR=3.22 (95% CI: 1.72, 6.04)]; Hispanic [OR=2.79 (95% CI: 1.51, 5.17)]; family history of asthma [OR=3.48 (95% CI: 2.34, 5.19)]; obese [OR=2.39 (95% CI: 1.43, 3.99)] and significant neighborhood traffic [OR=1.81 (95% CI: 1.10, 2.98)]. When the final model was stratified by sex, there was no association between neighborhood traffic and asthma/asthma like symptoms among females: OR=1.29 (95% CI: 0.60, 2.76) [n=417]. However, the males (n=438) had a statistically significant association OR=1.89 (95% CI: 1.03, 3.49).

### Other variables independently associated with asthma/asthma like symptoms

We examined factors such as mode of delivery (vaginal or Caesarian section), child's use of antibiotic medication in the past year, child's stay at the neonatal intensive care unit after birth and gestational age at delivery. Gestational age at delivery (range 30.1 to 42.7 weeks) was positively associated with reported asthma/asthma like symptoms (OR: 1.18; 95% CI: 1.03, 1.34) after controlling for all variables in the final model. Reported neighborhood traffic remained statistically significant in this model as well (OR: 1.67; 95%CI: 1.04, 2.67).

## Discussion

In this study, we sought to determine the prevalence of reported neighborhood traffic (a proxy for TRAP exposure) and its association with childhood asthma/asthma like symptoms. In this ECHO cohort 15% of the children were exposed to significant neighborhood traffic, and there was a marked racial/ethnic disparity, with exposure rates being 39.5% in non-Hispanic black children and 34.9% in Hispanic children. Similarly, there was a marked racial/ethnic disparity in the prevalence of past or current asthma/asthma like symptoms.

The results from our statistical models indicate that the odds of having asthma/asthma like symptoms for children with reported high neighborhood traffic was 78% higher than the odds for children without reported high neighborhood traffic. These results are in similar direction as the Dutch Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study, which examined associations between measured traffic-related air pollution and the development of asthma, allergy, and related symptoms in a prospective birth cohort.<sup>55</sup> The authors found air pollution measurements, specifically PM<sub>2.5</sub> concentrations, were associated with increased incidence of asthma [OR = 1.28 (95% CI: 1.10, 1.49)], prevalence of asthma [OR = 1.26; 95% CI: 1.04, 1.51], and prevalence of asthma symptoms [OR = 1.15 (95% CI, 1.02–1.28)]. These associations were even stronger for children who remained at their birth residence. The authors stressed the need for more birth cohort studies, since the role of air pollution exposures in the development of childhood asthma, allergy, and related symptoms remains unclear.

There has been mounting evidence of a causal effect of TRAP exposures on asthma exacerbations.<sup>56</sup> Our findings are consistent with the results of a prospective study in Sweden (n ~ 4000) which found positive associations between early life air pollution exposures (PM<sub>10</sub> and NO<sub>2</sub>) and asthma exacerbations.<sup>57</sup> The Cincinnati birth cohort study (n ~ 700) also detected associations between particulate air pollution exposure and wheezing during infancy.<sup>58</sup> Another study reported significant associations between traffic-related pollution and asthma exacerbations in children born to parents with atopic dermatitis and in those suffering from recurrent wheezing or asthma.<sup>59,60</sup> Our results adds to the growing evidence on the importance of relevant windows of TRAP exposure.

A 2017 meta-analysis of 41 epidemiologic studies provided evidence for the hypothesis that childhood exposure to TRAP contributes to the development of asthma, and called for further studies.<sup>61</sup> A recent review, based on seven studies, concluded that TRAP exposures may be associated with transient and persistent asthma/wheezing phenotypes in children,<sup>56</sup> and also stressed the need for more studies on these phenotypes. As children's early life and current exposures to TRAP appears to play a key role in asthma development,<sup>18</sup> carefully designed studies are needed to understand this relationship and identify critical windows for intervention.

Previous studies have assessed exposure to TRAP by directly measuring air pollutants, modelling, or indirectly by using distance to busy roads and/or self-reported traffic intensity.<sup>58,62–64</sup> A prospective cohort study of air pollution and respiratory health among children reported that incident asthma was

positively associated with TRAP measured outside children's residences for two weeks during the summer and winter.<sup>65</sup> Another birth cohort of racially diverse children (n = 24,608) reported an association between early-life mobile source models of air pollution and childhood asthma incidence.<sup>66</sup> A more recent study showed that decreased ambient air pollutants in Southern California between 1993 and 2014 was associated with a lower incidence of childhood asthma.<sup>67</sup>

In our study, we found that children of racial minority groups had a higher odds of asthma/asthma like symptoms when compared to non-Hispanic white children which is in agreement with prior reports.<sup>68-70</sup> The odds of asthma/asthma like symptoms for non-Hispanic Black and Hispanic children were 153% and 125% higher than the odds for non-Hispanic White children, respectively. This difference remained even after adjusting for mother's education as a proxy for socioeconomic status.<sup>71</sup> A recent U.S. Centers for Disease Control and Prevention Report showed that asthma prevalence is more than twice as high among African American children (15.7%) and nearly twice as high in children of Puerto Rican (12.9%) descent compared with non-Hispanic white children (7.1%).<sup>72,73</sup>

Our results further showed that asthma/asthma like symptoms was strongly associated with being male and having a positive family history of asthma. The odds of asthma/asthma like symptoms for males was 53% higher than for females. Other studies have also reported increased risk of asthma and asthma-related symptoms in males, when compared to females.<sup>74-76</sup> In our study, children with asthma/asthma like symptoms had more exposure to current secondhand smoke/environmental tobacco smoke (15.7% vs 9.6%). However, after adjusting for demographic factors, this effect was no longer significant. We did not observe differences between asthma/asthma like symptoms and the presence of cats and dogs either during the child's first year or in the last 12 months. These results are similar to a prior cohort study.<sup>59</sup>

We also found that obese children had 154% higher odds of having asthma/asthma like symptoms than non-obese children. Additionally, children with play equipment in the home environment/backyard had 60% higher odds of having asthma/asthma like symptoms than those without such items in the home environment. The presence of traffic can negatively affect physical activity in the neighborhood<sup>77,78</sup> a key determinant of obesity.<sup>63</sup> Two longitudinal studies have reported the possible contribution of air pollution exposure to the development of obesity in children<sup>63,79</sup> and animal studies support these observations.<sup>80,81</sup> Parents may opt to have play equipment within the home environment, such as in a backyard, to allow for physical activity, and that may be of benefit, especially for families residing in urban areas.<sup>82</sup> However, parents may also need to consider potential TRAP exposures that could occur during outdoor physical activity.

This is the first study to report significant positive associations between asthma/asthma like symptoms and play equipment in the home environment/backyard, even after adjusting for obesity. Children who had play equipment in their backyards had higher odds of asthma like symptoms while those who had access to local parks did not when obesity was added to our regression models. There may be several

reasons for this. The effect of green spaces on wheezing/asthma symptoms may depend on the size of the space, amount of vegetation, and types of pollution present.<sup>83 84 85</sup> In addition, parks must be safe for children to use. Studies have shown that regular physical activity has health benefits.<sup>86</sup> Additionally, other studies have shown that regular physical activity has health benefits for children when they are in low pollution rather than high pollution environments.<sup>87, 88</sup> While there is the possibility that playing in the backyard exposes a child to TRAP, further research is needed to examine the possible interplay of TRAP with exercise, types of green spaces, and obesity in relation to asthma/asthma like symptoms.<sup>89</sup>

Strengths of the study include the prospective longitudinal follow up of the children from mothers' first trimester through up to 8 years of age and the racial/ethnic diversity of the cohort. The ISAAC questionnaire is a validated tool and the Pre-PAQ has also been reported to be both a valid and reliable measure of parental, family and neighborhood factors.<sup>49</sup> As such, we expect little misclassification, if any.

Our study also has several limitations. First, data are from maternal response to questionnaires and therefore subject to recall bias. However, we believe this bias was equally distributed among children with and without reported asthma/asthma like symptoms, biasing effect estimates toward the null hypothesis. This is because the Pre-PAQ questions in this study assessed children's physical activity and not specific environmental exposures. An analysis comparing the current participants in the study with the participants who were eligible for the study revealed statistically significant differences in maternal race-ethnicity and education; however, participants were similar with respect to maternal age, child sex, gestational age at delivery, year of birth and birthweight (Supplementary Table 1). We also believe that controlling for child's race-ethnicity as well as maternal education mitigated any impact of potential selection bias and results remain informative. In our study, there was an association between reported asthma/asthma like symptoms and increased gestational age at delivery, but not for other factors such as mode of delivery, child's use of antibiotic medication in the past year of child's stay at the neonatal intensive care unit after birth. While early-term birth is a predictor of asthma, late term birth has also been associated with atopic dermatitis by 7 years of age<sup>90</sup>. Atopic dermatitis often precedes other allergic diseases such as asthma<sup>91</sup>, however, given the cross sectional nature of our study, we are limited in discussing this topic. We concur with the strong need to identify alternatives for disease prevention<sup>91</sup>. There may also be genetic differences in the children enrolled in this study and this may affect susceptibility to TRAP. Since our analysis is cross-sectional, we are unable to determine whether exposure to TRAP preceded respiratory symptoms, or vice-versa, as such reverse causality is possible, as well as the possible time-related effects of obesity. Hence we had limited power to fully delineate some potential associations.

Finally, our exposure variable of interest, significant neighborhood traffic, was determined by questionnaire responses from mothers and we did not attempt to conduct air pollution exposure assessment outside their residences. Future directions for this work will involve investigations with historical records of ambient air pollution, particularly during the pre and post-natal periods, as well as

lung function data. Clinicians should look closely at the contribution of an environmental factor such as traffic-related air pollution among patients who experience asthma/asthma like symptoms to prevent deteriorating pulmonary health. Additionally, public health professionals may also need to improve surveillance to help identify communities which may be at risk for increased TRAP concentrations.

## **Conclusion**

Our findings provide evidence that there is a significant association between reported significant neighborhood traffic and asthma/asthma like symptoms among children in the ECHO cohort. Minority status, male sex, the presence of play equipment within the home environment, family history of asthma and obesity were also associated with asthma/asthma like symptoms, highlighting the complexity of environmental and genetic interactions influencing lung function. Further studies are needed since many children, particularly minority children at high risk of asthma, may live in close proximity to this source of environmental air pollution.

## **Declarations**

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## Contributions

SC wrote original draft. RN, RW, JV and KJH made substantial contribution in study design and methodology. PF cleaned up data set and edited the draft, BN, WB, AT, JP, MB, ES, JR, DS, AS, KP and RM aided in data interpretation and edited the draft. All authors read and approved the final manuscript.

## Ethics approval and Consent to participate

During recruitment, parents received detailed information regarding the purposes of the project and were given the opportunity to voice any concerns and/or to sign the informed consent. The study utilized a central IRB (cIRB) through Columbia University for all ten participating sites. A SMART IRB Master Common Reciprocal Institutional Review Board Authorization Agreement ("SMART IRB Agreement") was used to establish reliance between the participating sites and the Columbia University IRB. The study was conducted in accordance with the standards of Good Clinical Practice. Written informed consent was obtained from the parents or legal guardians of each enrolled child.

## Consent for publication

Not applicable.

## Competing interests

The authors declare that no competing interests exist.

## Availability of supporting data

Data contains personal health information and cannot be made publicly available. Data can be available from the authors upon reasonable request, with permission of NICHD and with establishment of required data use agreements. Any data inquiries are referred to the corresponding author (scommod@iu.edu) or PI (huntke@musc.edu).

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## Figures

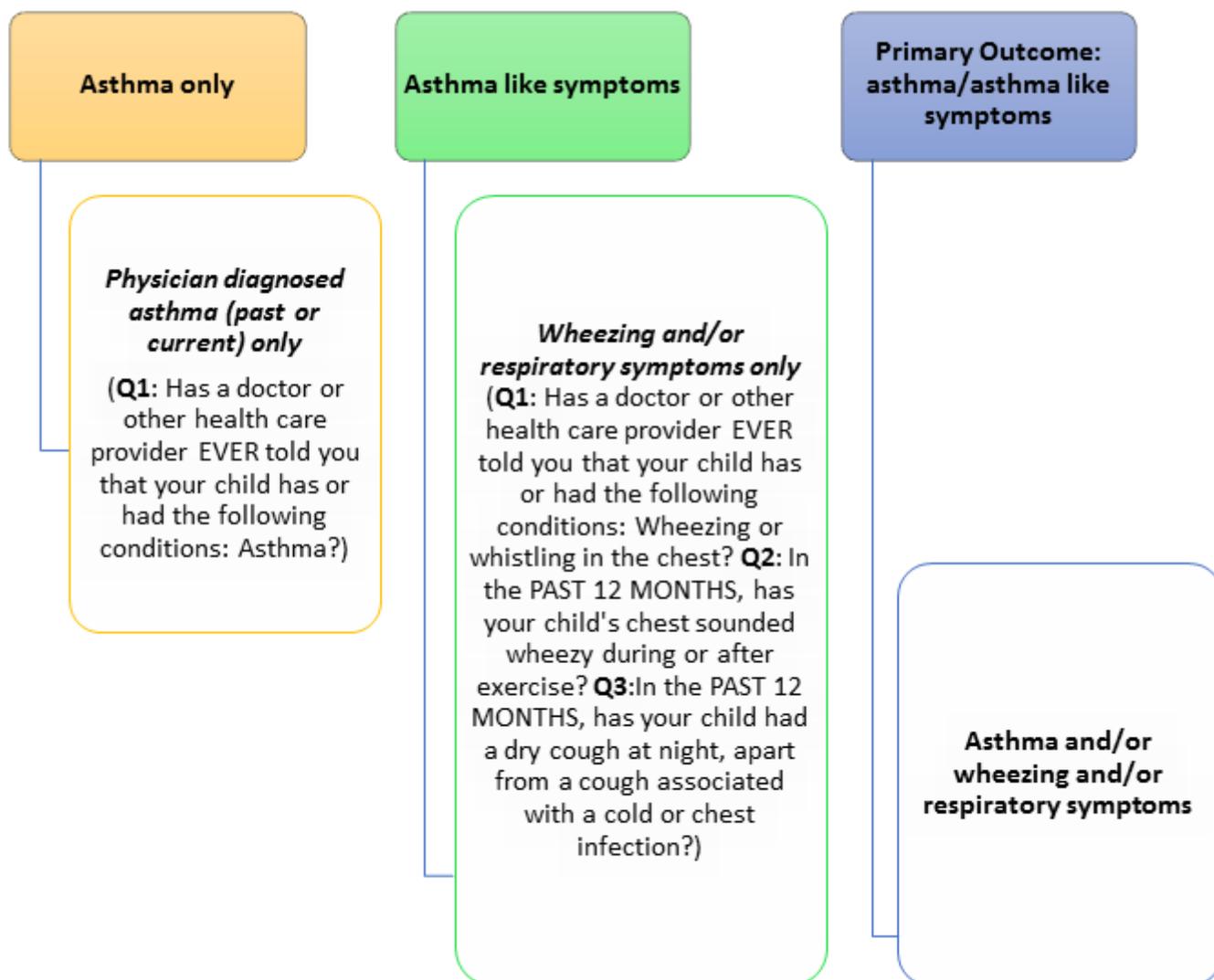


Figure 1

Definition of primary outcome: asthma/asthma like symptoms.

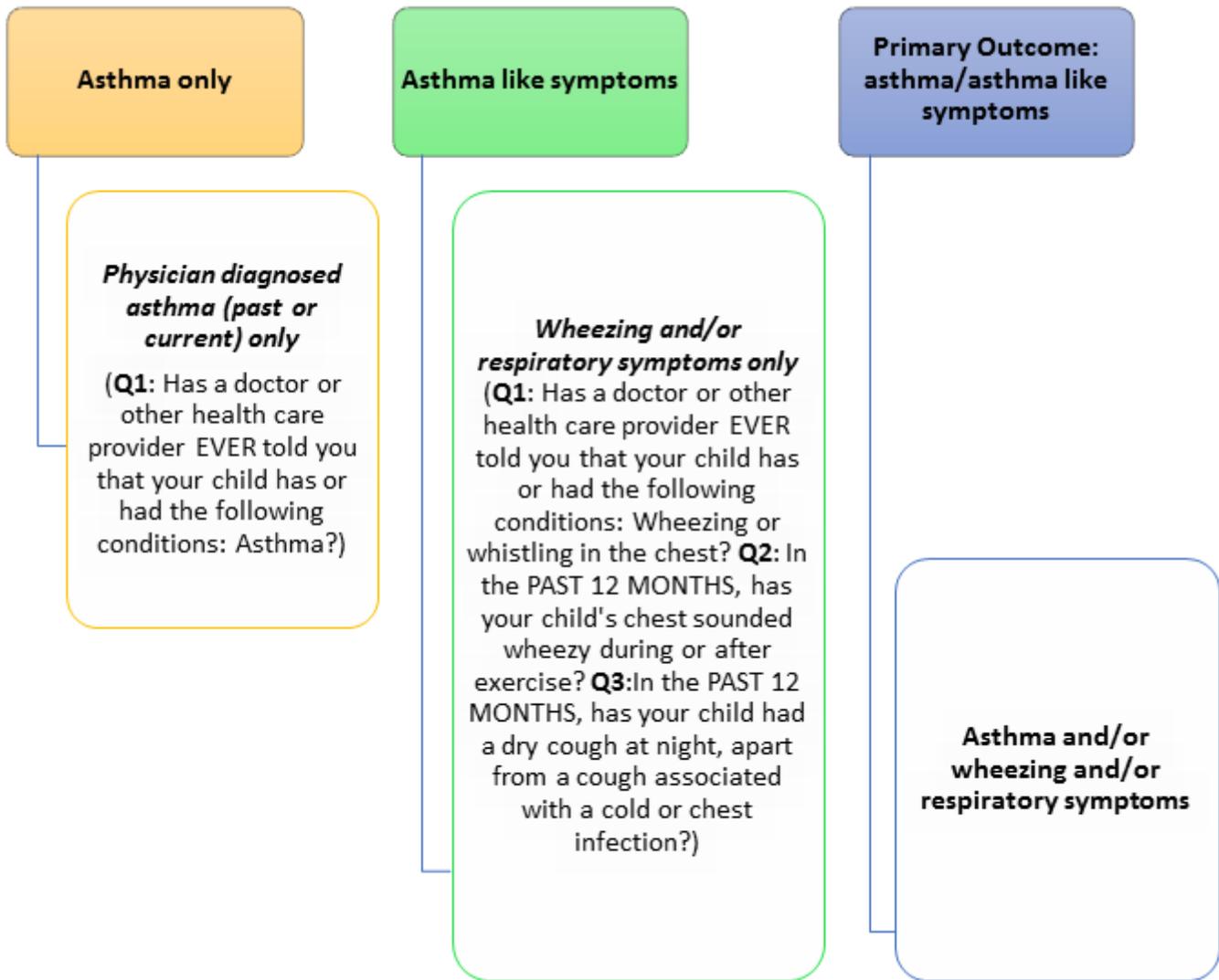
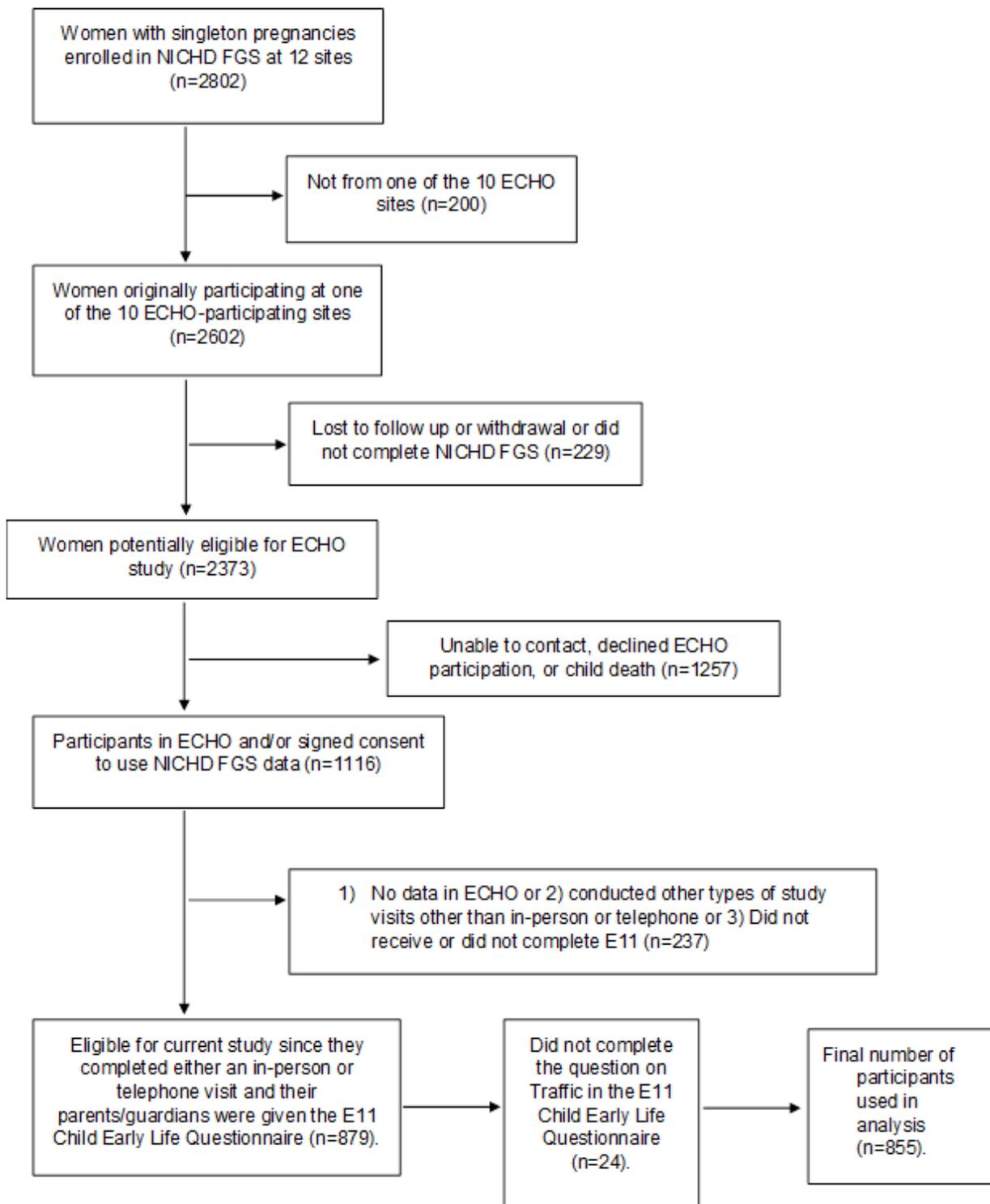


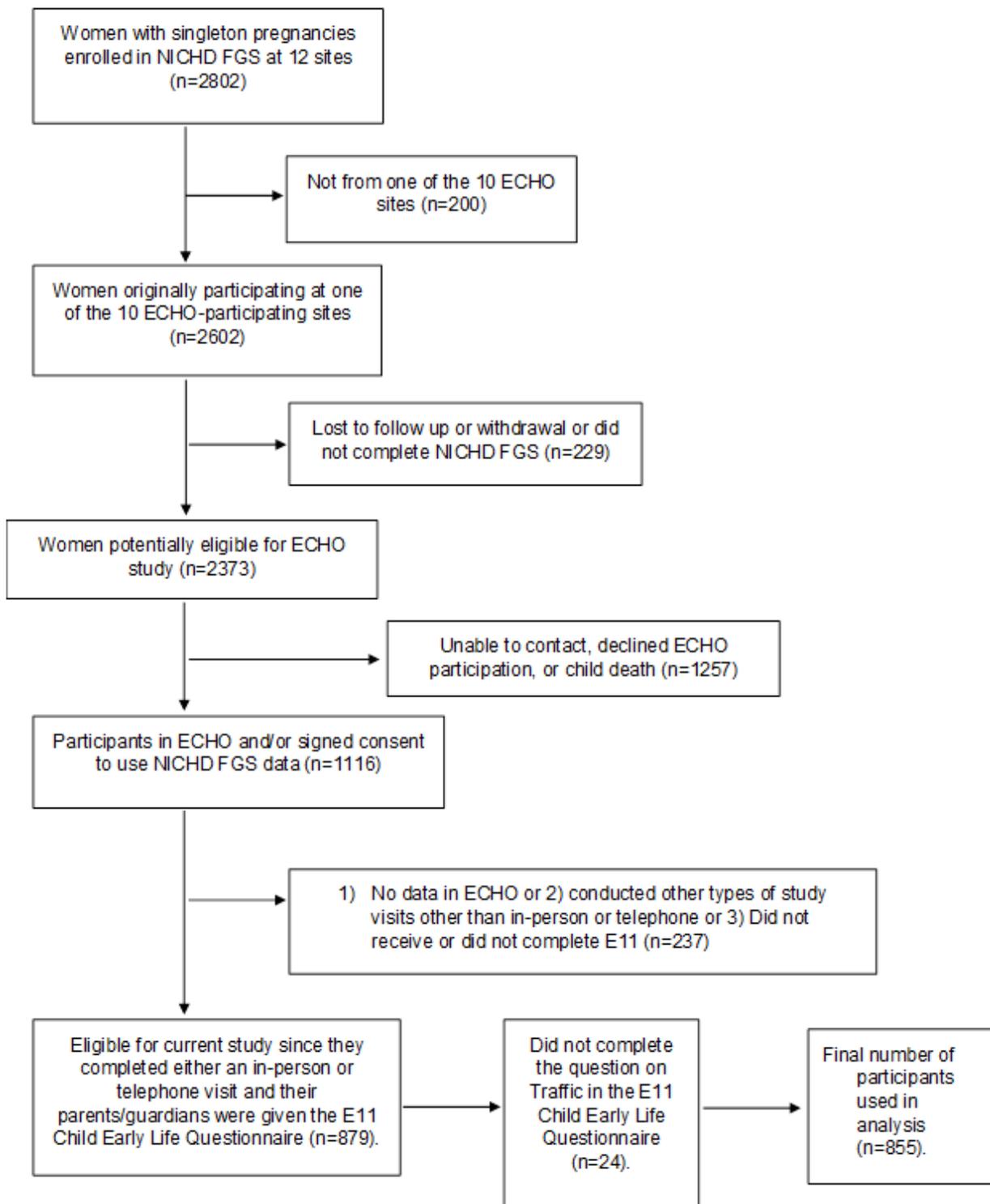
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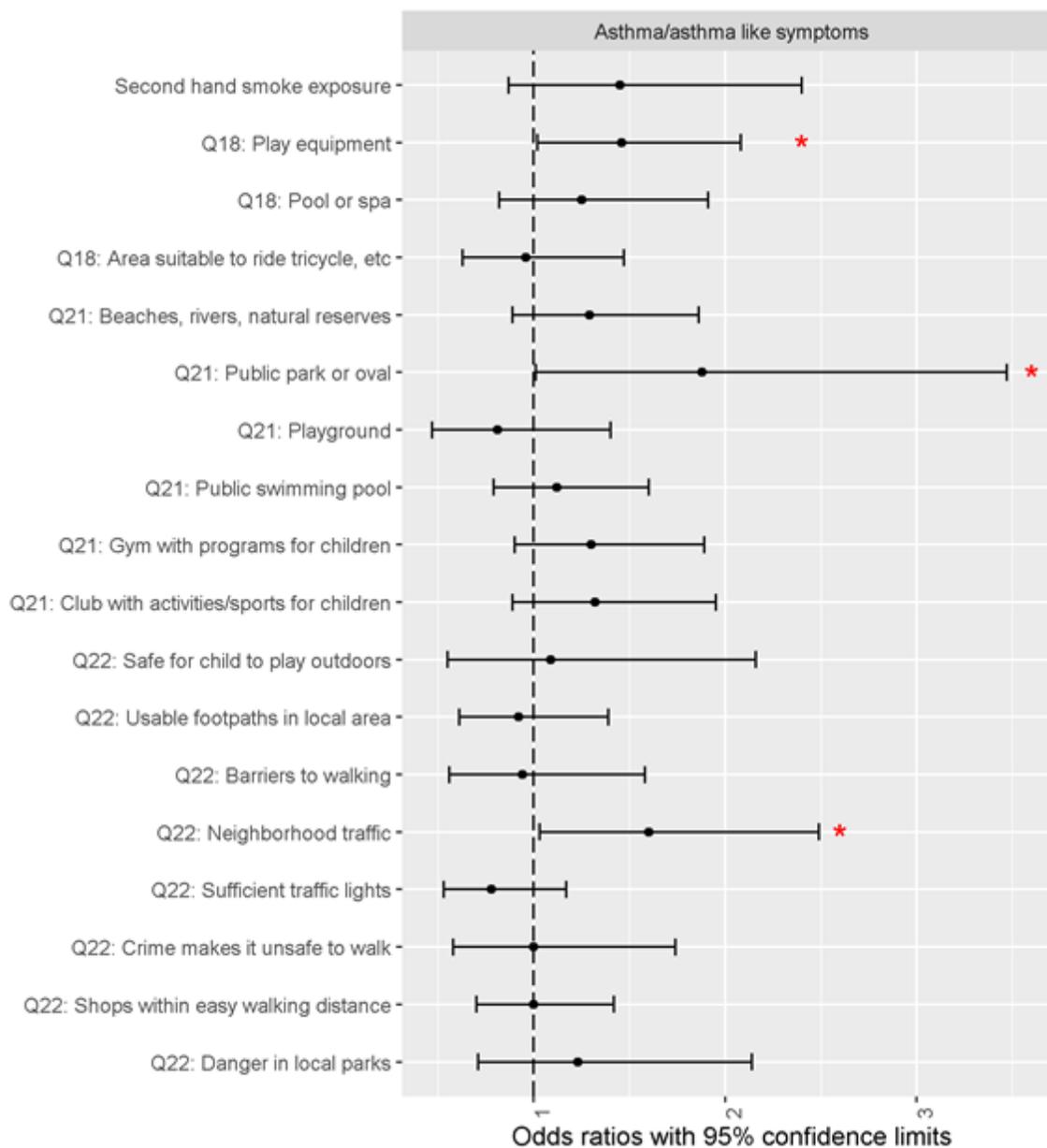
**Figure 2**

Sample size used in the present study in relation to the original Eunice Kennedy Shriver NICHD Fetal Growth Studies cohort.



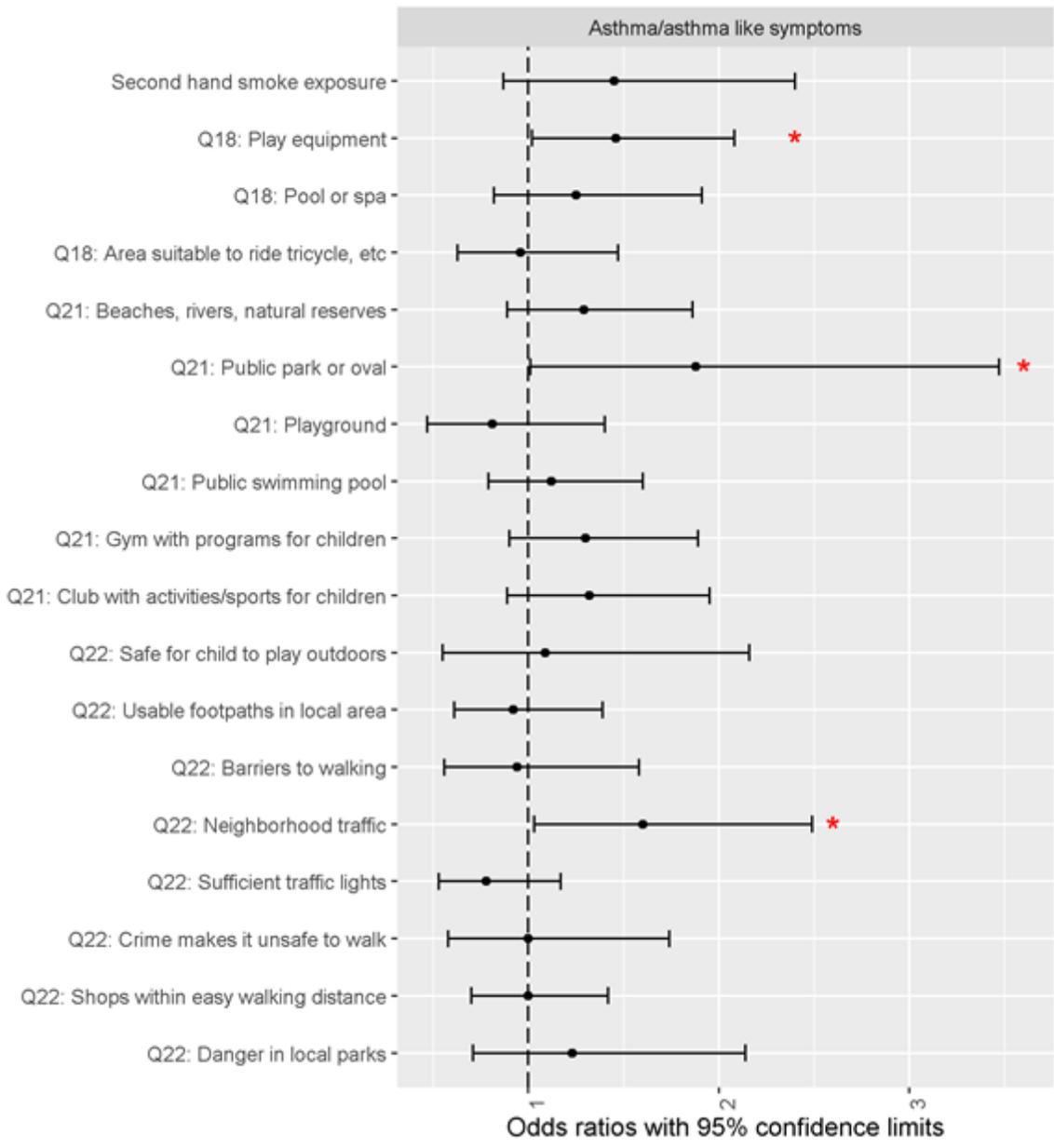
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Sample size used in the present study in relation to the original Eunice Kennedy Shriver NICHD Fetal Growth Studies cohort.



**Figure 3**

Odds ratios estimates with 95% confidence limits for individual covariates of interest for asthma/asthma like symptoms, including secondhand smoke exposure as well as each of the Pre-PAQ Q18, Q21 and Q22 variables. Each covariate was in a separate logistic regression model, and the OR estimates are adjusted for child sex, child age, race-ethnic group, mom education and family history of asthma. Red asterisk indicates statistically significant result.



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Odds ratios estimates with 95% confidence limits for individual covariates of interest for asthma/asthma like symptoms, including secondhand smoke exposure as well as each of the Pre-PAQ Q18, Q21 and Q22 variables. Each covariate was in a separate logistic regression model, and the OR estimates are adjusted for child sex, child age, race-ethnic group, mom education and family history of asthma. Red asterisk indicates statistically significant result.