

RESEARCH ARTICLE

Investigating the relationships among neighborhood factors and asthma control in African American children: A study protocol

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ABSTRACT

Over 2 million children in the US have uncontrolled asthma. African American children are disproportionately affected with a risk of dying from asthma that is 7.6 times higher than non-Hispanic White children. Racial disparities in childhood asthma are partially attributed to differential exposures to poverty; unsafe and stressful neighborhoods; and unhealthy physical environments. This paper describes the protocol for an ongoing National Institutes of Health/National Institute of Nursing Research-funded descriptive, cross-sectional study to investigate two neighborhood factors that may influence children's asthma. Building on an existing dataset, this study examines associations among neighborhood greenspace, neighborhood safety, and level of asthma control while controlling for indoor asthma triggers in an urban sample of predominantly low-income, African American children with persistent asthma. Two new variables are added to the dataset: availability of neighborhood greenspace and neighborhood violent crime rate. Greenspace is being accessed using geographic information systems and measured using the normalized difference vegetation index. Neighborhood violent crime rate is calculated using geocoded, point locations for crimes downloaded from the city police department. It is hypothesized that parents living in unsafe neighborhoods are likely to keep their children indoors, thereby increasing their children's exposure to indoor asthma triggers and limiting the potential benefits of neighborhood greenspace. The biggest challenges thus far are related to limited variability in greenspace and violent crime rates. Progress to date and strategies to address these challenges are discussed. Results have the potential to inform interventions to improve asthmatic children's health and influence public health policy.

KEYWORDS

childhood asthma, greenspace, neighborhood and built environments, neighborhood safety

1 | INTRODUCTION

Currently 6.1 million children in the United States have asthma, with an estimated total cost of \$81.9 billion annually in healthcare related expenditures and costs incurred by absenteeism and mortality (Nurmagambetov, Kuwahara, & Garbe, 2018; Zahran, Bailey, Damon, Garbe, & Breyse, 2018). Approximately 38% of these children have

uncontrolled asthma defined as having two or more symptom days per week, more than one symptom night per month, activity limitation, and use of rescue medications more than 2 days per week (U.S. Department of Health and Human Services & National Heart, Lung, and Blood Institute, 2007; U.S. Department of Health and Human Services, Center for Disease Control and Prevention, & National Center for Environmental Health, 2015). Children with uncontrolled

asthma use more healthcare resources and report lower quality of life when compared to children with controlled asthma (Braido, 2013). The burden of asthma is not equally distributed across racial groups. According to a recent Centers for Disease Control and Prevention report, 22.5% of African American children with asthma had an asthma-related emergency department visit in the past year compared to 12.2% of non-Hispanic white children with asthma (Zahran et al., 2018).

Racial disparities in asthma outcomes are likely attributable, in part, to differential exposures to neighborhood conditions because segregation and economic disadvantage influence neighborhood residence. These exposures include unhealthy physical environments, such as air pollution, poor quality of housing stock, presence of pests in the home, and exposure to secondhand smoke, and unhealthy social environments, due to violence and stress (DePriest & Butz, 2017). For example, children from low-income families are exposed to higher levels of traffic related air pollution; live in lower quality, more crowded, and noisier homes; and are exposed to more neighborhood violence compared to children from more affluent families (Evans & Kim, 2013).

Neighborhood-level factors, including air pollution, poor housing stock, crime and violence, are shaped by both political and economic factors and can be difficult to change (Gomez, 2016). However, one potentially modifiable factor that may improve asthma control is the availability of greenspace, defined as land with grass, trees, or other vegetation (U.S. Environmental Protection Agency, 2016). Prior research indicates that neighborhood greenspace is associated with greater physical activity and social connection and with lower levels of perceived stress, environmental heat and air-pollution, variables that have been associated with asthma control in children (Hartig, Mitchell, de Vries, & Frumkin, 2014; Tosca, Ruffoni, Canonica, & Ciprandi, 2014; Wanrooij, Willeboordse, Dompeling, & van de Kant, 2014). Indeed, some studies have shown that increases in the "normalized difference vegetation index" or NDVI, a measure of the greenspace in a given geographical area, is associated with decreased asthma prevalence (Sbihi, Tamburic, Koehoorn, & Brauer, 2015). However, other studies have shown no effects or negative effects of greenspace on asthma prevalence and control (Dadvand et al., 2014; Fuertes et al., 2016). One possible explanation for the mixed results is the failure to account for indicators of neighborhood safety, such as neighborhood violent crime rate and parent perceptions of neighborhood safety, which would affect parents' willingness to allow their children to use greenspace. Living in an unsafe neighborhood has been associated with greater stress and children spending less time outside resulting in increased exposure to indoor allergens and pollutants, including second hand smoke (Datar, Nicosia, & Shier, 2013; Kanchongkittiphon, Mendell, Gaffin, Wang, & Phipatanakul, 2015). Research has demonstrated poor asthma control in areas with high violent crime compared to similar areas with low violent crime (Beck et al., 2016). The purpose of this paper is to describe the protocol for a National Institutes of Health/National Institute of Nursing Research-funded study examining the associations among greenspace, neighborhood safety, and asthma control, while controlling for indoor asthma triggers, in children with asthma living in urban poverty.

2 | BACKGROUND

2.1 | Low-income, African American children are disproportionately affected by asthma

Asthma is the most common cause of all pediatric emergency department (ED) visits (Akinbami et al., 2012). Repeated ED visits are an index for poorly controlled asthma as children with frequent ED visits are at the greatest risk for life-threatening asthma, decreased quality of life, and increased school absences (U.S. Department of Health and Human Services & National Heart, Lung, and Blood Institute, 2007). Uncontrolled asthma also leads to inflammation and airway remodeling that may contribute to long-term loss of lung function and impairment (Grainge et al., 2011). Low-income, African American children with asthma have 4.1 times more ED visits and a death rate that is 7.6 times higher than that of non-Hispanic White children (Akinbami, Moorman, Garbe, & Sondik, 2009). There is strong evidence that environmental exposures are important contributors to high rates of asthma-related morbidities (Meyers, Bleecker, Holloway, & Holgate, 2014). Environmental factors such as chronic exposures to indoor allergens, secondhand smoke, air pollution, violence, and toxic stress; sedentary lifestyles; and obesity are differentially distributed according to economic disadvantage (Forno & Celedón, 2009). Limited access to guideline-based preventative care in low-income underserved communities also contributes to higher rates of uncontrolled asthma (Butz, Kub, Bellin, & Frick, 2013). The National Asthma Education and Prevention Program Expert Panel Report 3, published by the National Heart, Lung, and Blood Institute (NHLBI), identified a history of "low socioeconomic status or inner-city residence" as a key risk factor for asthma-related mortality (U.S. Department of Health and Human Services & National Heart, Lung, and Blood Institute, 2007). Baltimore City has the highest rate of pediatric asthma hospitalizations in Maryland and one of the highest in the nation (Kelly & Burkhart, 2017). Identifying modifiable factors that can lead to improved asthma control among African American children growing up in urban poverty has been named a research priority by the Environmental Protection Agency, Healthy People 2020, and supports the National Institute of Nursing Research's goal to understand environmental determinants of health in those with chronic disease (United States Department of Health and Human Services, 2016a; United States Department of Health and Human Services, 2016b; United States Environmental Protection Agency, 2016a,b).

2.2 | Availability of greenspace may be a protective factor for children with asthma

Greenspace in an urban environment has been shown to decrease environmental heat and air-pollution (Nowak, Crane, & Stevens, 2006). Greenspace has also been associated with increased physical activity and social connection and reduced stress and obesity (Hartig et al., 2014). Given that heat, air pollution, obesity, stress, and a sedentary

lifestyle are all linked with poorer asthma control some researchers have started to examine whether the availability of greenspace is associated with lower prevalence of asthma and better asthma control (Quinto et al., 2011). See Figure 1 for the conceptual framework of these relationships.

Several studies have examined the relationship between greenspace and asthma prevalence rates. Although some studies have found significant relationships suggesting greenspace may reduce asthma rates (Lovasi, Quinn, Neckerman, Perzanowski, & Rundle, 2008; Sbihi et al., 2015), the few that looked at asthma control did not find significant effects (Chen et al., 2017; Lovasi et al., 2008). Although asthma rates are important health indicators, rates of asthma control are stronger indicators of morbidity and mortality risk (U.S. Department of Health and Human Services & National Heart, Lung, and Blood Institute, 2007). This study examines associations between greenspace and indicators of the level of asthma control in a low-income, high-risk pediatric population.

It is important to note that not all studies that have examined the relationship between greenspace and asthma prevalence have uncovered a significant health effect (Dadvand et al., 2014; Pilat et al., 2012). Some studies with non-significant results were conducted in small cities where asthma rates were low, which may have contributed to floor effects (Quinto et al., 2011). Another study was limited by using tree canopy, rather than a stronger measure of greenspace, such as NDVI (Lovasi et al., 2008). NDVI is a validated, practical measure of greenspace (Rhew, Vander Stoep, Kearney, Smith, & Dunbar, 2011). None of the prior studies controlled for the effects of neighborhood safety. This study uses NDVI to measure neighborhood greenspace in a city with higher than average rates of both pediatric asthma and neighborhood violence.

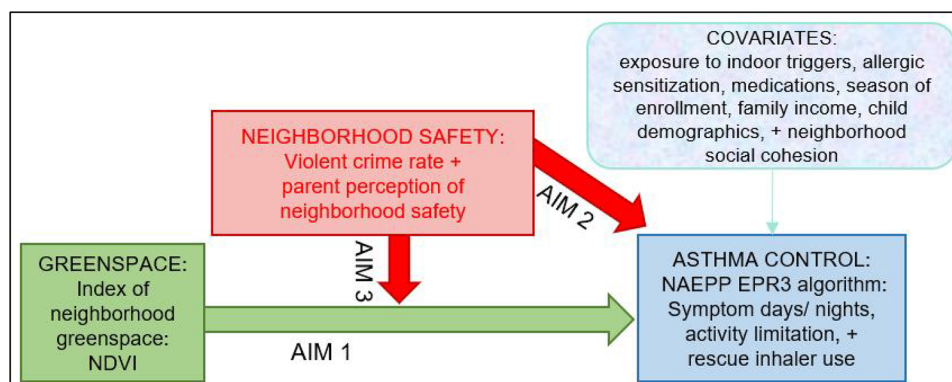
To date, no study has investigated the association between greenspace and pediatric asthma control in low-income, segregated, urban communities. This study will address the limitations of previous studies by (a) employing a validated method (NDVI) for estimating neighborhood greenspace; (b) focusing on a sample of children at

greatest risk for asthma-related morbidity and mortality (i.e., African American children living in urban poverty); and (c) examining the relationship between the availability of neighborhood greenspace and asthma control based on the parent report of symptoms, activity limitations and rescue inhaler use for the child in the preceding weeks.

2.3 | Neighborhood safety may be a potentially important modifying factor that prevents the use of greenspace

Markers of neighborhood safety such as violent crime, which tend to be higher in low-income, segregated neighborhoods (Williams, Sternthal, & Wright, 2009), may limit the benefits of greenspace on children's asthma control as parents may be less likely to allow their children outdoors. Neighborhood safety can be captured objectively using neighborhood violent crime statistics and subjectively using parents' perceptions of neighborhood safety. Although it is likely these two estimates of neighborhood safety are related because parents acquire perceptions of neighborhood safety, at least in part, based on the amount of violent crime occurring in their neighborhood, parent perceptions of neighborhood safety may be a stronger predictor of child health outcomes. For example, neighborhood crime statistics capture averages by designated community statistical areas (CSAs). However, parents may base their assessments of neighborhood safety on a different concept of where their neighborhood falls, a single incident that occurred in an otherwise low-risk neighborhood, or a personal encounter with violence, that may not be reflected fully in CSA crime statistics.

Parents who perceive their neighborhoods as unsafe are likely to keep their children indoors, which would reduce the risk of harm but also increase their exposure to indoor asthma triggers including cockroaches, mice, rats, and secondhand smoke; and limit their physical activity (Carver, Timperio, & Crawford, 2008; Kanchongkittiphon et al., 2015; Quinto et al., 2011). Research has demonstrated a link between parent



NDVI = normalized difference vegetation index; NAEPP EPR3 = National Asthma Education and Prevention Program. Expert Panel Report 3

FIGURE 1 Conceptual model. This model shows the hypothesized relationships between independent and dependent variables, measurement of variables, covariates to be considered in data analysis as well as the relationship that each specific aim will investigate

perception of the neighborhood as unsafe and poor asthma control (Bellin et al., 2014; Kopel et al., 2015). Parent perception of neighborhood safety may also affect the parent's level of stress leading to unhealthy coping behaviors such as smoking, which is more common in low-income, urban communities (Wright & Subramanian, 2007). Secondhand smoke exposure is also a known trigger for children with asthma (Kanchongkittiphon et al., 2015; Lang et al., 2013).

Unsafe neighborhoods can also increase child stress thereby affecting the inflammatory response (Janusek, Tell, Fishe, Gaylord-Harden, & Mathews, 2012). For example, asthmatic children exposed to acute stressors have increased airway inflammation, an effect found to be greatest among low-income children (Marin, Chen, Munch, & Miller, 2009). Over time chronic stress exposure can modify the hypothalamic-pituitary-adrenal axis which alters the way individuals respond physiologically to asthma triggers, prompting more frequent exacerbations (Rosenberg, Miller, Brehm, & Celedón, 2014). In two studies utilizing violent crime statistics, areas with higher violent crime rates had higher numbers of asthma ED visits in Cincinnati (Beck et al., 2016) and higher asthma prevalence in Chicago (Gupta et al., 2010) compared to areas in the same cities with lower violent crime rates. This body of research, predominantly done in low-income communities, demonstrates a link between safety and asthma control but fails to control for exposure to indoor triggers.

This study controls for indoor triggers and examines two different indicators of neighborhood safety, neighborhood violent crime statistics and parent perception of neighborhood safety, to determine if one measure is a stronger predictor of asthma control. If parent perception of neighborhood safety is a stronger predictor of asthma control than neighborhood crime statistics, it may suggest that parent stress and perceptions play a more important role in understanding how neighborhood factors affect children's asthma control. Looking at these indicators of neighborhood safety separately will inform future research into differing mechanisms of the association between neighborhood safety and asthma control. This study is also the first to analyze neighborhood safety as a potential modifier in the relationship between greenspace and asthma control. These relationships are depicted in Figure 1. Research accounting for the larger context of neighborhood environment including neighborhood safety will inform more effective implementation of greenspace initiatives in urban areas with high rates of poverty, violence, and asthma like Baltimore.

3 | RESEARCH DESIGN AND METHODS

3.1 | Study design

This study uses a cross-sectional design to analyze the role of neighborhood safety in understanding the extent to which the availability of greenspace may benefit children with asthma living in urban poverty.

Building on an existing randomized controlled trial of parents of children with asthma (Butz et al., 2015), this study uses multiple measures and informants to capture study variables

including geocoding, neighborhood crime statistics, parent reports, and physiologic measures. Data analysis will control for indoor asthma triggers as well as season of baseline data collection. In a sample of 222 predominantly African American, low-income children living with asthma in Baltimore City the specific aims of this study are:

3.1.1 | Specific aim 1

Examine the association between neighborhood greenspace and level of asthma control.

Hypothesis 1: Lower index of neighborhood greenspace (measured as NDVI) will be associated with poor asthma control.

3.1.2 | Specific aim 2

Examine the associations among neighborhood safety, measured as neighborhood violent crime rate and parent perception of neighborhood safety, and level of asthma control. Hypothesis 2A: Higher rates of neighborhood violent crime will be associated with poor asthma control; Hypothesis 2B: Parent perception of an unsafe neighborhood will be associated with poor asthma control. Hypothesis 2C: Parent perception of neighborhood safety will be more strongly associated with level of asthma control than neighborhood violent crime rate.

3.1.3 | Specific aim 3

Explore neighborhood safety (neighborhood violent crime rate and parent perception of neighborhood safety) as a potential moderator in the association between neighborhood greenspace and level of asthma control. Hypothesis 3: Neighborhood safety will moderate the relationship between greenspace and level of asthma control.

3.2 | Sampling and recruitment

The data set for the current study includes baseline data collected from 222 parent/child dyads enrolled in a study testing the efficacy of a behavioral intervention for improving pediatric asthma control (Butz et al., 2015). These parent/child dyads were recruited August 2013 through February 2016 after presenting to the Johns Hopkins Hospital Pediatric Emergency Department due to asthma exacerbation. Child inclusion criteria were (a) physician diagnosed asthma; (b) ≥ 2 ED visits or 1 hospitalization for asthma within the past year; (c) mild to severe persistent asthma based on NHLBI criteria (U.S. Department of Health and Human Services & National Heart, Lung, and Blood Institute, 2007); (d) 3–12 years old; (e) resides in Baltimore City; and (f) they or a sibling are not currently participating in an asthma study. Child exclusion criteria were (a) inability to speak and understand English; (b) no access to a working phone for follow-up surveys; (c) co-morbid respiratory condition; and (d) situation where consent cannot be obtained from legal guardian. Parent/legal guardian inclusion criteria were (a) parent/legal guardian of child with asthma age 3–12 years

attending the Johns Hopkins Hospital Pediatric Emergency Departments for acute asthma treatment and the child meets inclusion criteria above; (b) reside in Baltimore City; (c) ability to read at basic or 4th grade level. Reading level was tested during the consent process by asking the consentee to read a part of the consent. Parent/legal guardian exclusion criteria were (a) inability to speak and understand English and (b) no access to a working phone for follow-up surveys. If criteria were met, parents were consented, and children age 7–12 years signed a written assent form. Parents were remunerated \$30 for baseline survey participation. The parent study and the current study were both approved by the Johns Hopkins Medicine institutional review board.

3.3 | Neighborhood level data

Conceptually, the neighborhood is defined as an overlapping area of ecological units varying in size (e.g., a block is smaller than a census tract) and including an inconsistently interacting group of people and institutions (Sampson, Morenoff, & Gannon-Rowley, 2002). For this research, neighborhood will be operationalized as community statistical area (CSA). The Baltimore City CSAs were defined originally by the Baltimore Data Collaborative with the Baltimore City Department of Planning to provide a consistent representation of the conditions within particular neighborhoods (Baltimore Neighborhood Indicators Alliance-Jacob France Institute, 2015). The CSAs align with census tracts and reflect the City planner's understanding of residents' perception of the boundaries of the community (Baltimore Neighborhood Indicators Alliance-Jacob France Institute, 2015). There are 55 CSAs in Baltimore City. Other studies have used census tracts or zip codes to define neighborhood boundaries, but research shows the results are robust to different methods of operationalizing neighborhood boundaries (Sampson et al., 2002). Participant addresses were geocoded using ArcGIS software (ESRI, 2010). Refer to Figure 2 for the geocoded map containing Baltimore City CSAs, participant locations, and asthma control for each participant. Once geocoded, using a spatial join in ArcGIS, the addresses were assigned to their CSAs for analysis.

3.4 | Variables and measures

Table 1 presents the study variables, measures, informant/source, evidence of reliability/validity, and whether the data were collected for the parent study ("Existing Data") or obtained for this protocol ("New Data").

3.4.1 | Asthma control (existing data)

Consistent with national guidelines, asthma control was calculated based on caregiver report of (1) the number of symptom days over the past 14 days; (2) the number of symptom nights over the past 30 nights; (3) activity limitation over the past week; and (4) short-acting β_2 -agonist use over the past 2 weeks (U.S. Department of Health and Human Services & National Heart, Lung, and Blood Institute, 2007). These variables were included in an algorithm to

categorize each child by whether their asthma was poorly controlled (yes or no).

3.4.2 | Asthma triggers and allergen sensitization (existing data)

At baseline, 5 ml of the child's blood was drawn to measure IgE antibodies to ten common environmental allergens: mouse, cockroach, cat, dog, timothy grass, *alternaria* and *aspergillus* molds, oak tree, common ragweed, and house dust mite. Saliva was also collected (1 ml) to measure salivary cotinine concentration, a biomarker for the child's level of nicotine exposure in the past 24 hr. Parents were asked if they had seen roaches, rats, or mice in their home in the past three months. These data were included as potential covariates.

3.4.3 | Family background information (existing data)

During enrollment parents filled out the baseline questionnaire to collect data on demographics, asthma medication use, daily stress, home asthma trigger exposures and perceived neighborhood safety. During this time parents were also asked their home address and period of time they had resided at their home address.

3.4.4 | Greenspace (new data)

Greenspace was calculated by determining the NDVI. This index, ranging from −1 to 1 with higher numbers indicating more greenness, has been shown to accurately measure the proportion of ground covered by green vegetation (Jackson & Huete, 1991). NDVI was derived from the Landsat Enhanced Thematic Mapper Plus (ETM+) data at 30 m by 30 m resolution (Dadvand et al., 2012). The ETM+ Landsat data were downloaded for the Baltimore City region for 2013, the first year of study enrollment, from the U.S. Geological Survey (<https://lta.cr.usgs.gov/LETMP>). NDVI was calculated by pixel and averaged for each CSA.

3.4.5 | Neighborhood violent crime rate (new data)

Geocoded point locations for victim-based crimes supplied by the Baltimore City Police Department were downloaded from Open Baltimore (<https://data.baltimorecity.gov/>). These data were downloaded for the years 2013, 2014, and 2015 and were stratified to include violent crimes, per the Federal Bureau of Investigation's Uniform Crime Reporting Program (United States Department of Justice, 2016), comprising homicide/manslaughter, rape, aggravated assault, and robbery. Violent crime rate was calculated by year by dividing the number of crimes recorded by the population in each CSA.

3.5 | Power analysis

The power analysis, conducted prior to addition of GIS data, was based on preliminary analyses of the distribution of level of asthma control in

Community Statistical Areas and Participant Addresses in Baltimore, Maryland

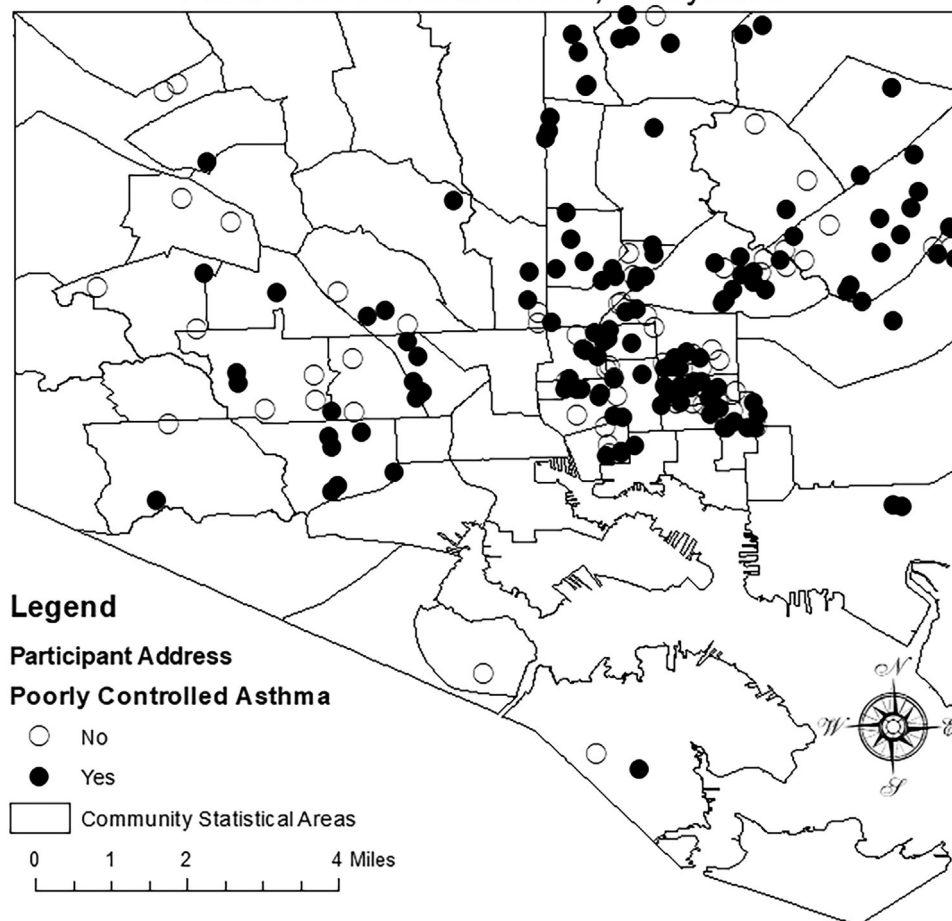


FIGURE 2 Map of Baltimore city separated into community statistical areas. The map includes the approximate location of each study participant and the symbol indicates the child's level of asthma control

the data set. Assuming that the variables NDVI and violent crime rate will be skewed (Beck et al., 2016; Davdand et al., 2014), these variables will be dichotomized to low versus high. Of the 222 children, 63.5% have poorly controlled asthma and 36.5% do not. Using this rate for the outcome and varying the intra-class correlation associated with CSA and percent with high greenspace or rate of violence (predictor variable) determined the odds ratio detectable with statistical power of 0.80, alpha level of 0.05, and $N = 222$. Table 2 summarizes the results for predictors of asthma control based on the distribution. For example, if greenspace is distributed as 50 percent high greenspace and 50 percent low greenspace, and the intra-class correlation coefficient is 0.10, the study is powered to detect an odds ratio of 2.17. The predictor distribution can also be used to determine detectable odds ratios depending on the distribution of violent crime rate (low vs. high). For the continuous predictor of caregiver perception of safety, significant odds ratios are detectable at 1.55, 1.52, and 1.49 if the ICC is 0.20, 0.15, and 0.10, respectively assuming power of 0.80, alpha of 0.05 and sample size of 222.

3.6 | Procedures

Building upon baseline data, home address was used to geocode the child's place of residence using the geospatial referencing software, ArcGIS version 10.5.1 (ESRI, 2010). NDVI data were added for 2013 using satellite imagery from April 2013. This image was chosen because it was during a green month with limited cloud cover over Baltimore City. Regardless of date of enrollment all participants have corresponding NDVI values calculated from the April 2013 data. Previous research demonstrates that measurement of NDVI is stable over several years (Dadvand et al., 2012). Neighborhood violent crime rate for 2013, 2014, and 2015 was assigned to each child depending upon their year of enrollment into the study. If the child was enrolled August 2013 through June 2014, they were assigned the violent crime rate from 2013; those enrolled from July 2014 through June 2015 were assigned the rate from 2014; and those enrolled from July 2015 through February 2016 were assigned the rate from 2015. Length of time at their home address will be included as a potential covariate during data analysis.

TABLE 1 Variables and measures

Variable	Measurement	New (N) or existing (E) data	Informant/Source
Dependent			
Asthma control—Aims 1, 2, and 3	Binary: poorly controlled (yes/no); Asthma Control Questionnaire test-retest reliability $r = 0.77$; criterion validity demonstrated by significant associations with clinicians' ratings of asthma control $r = 0.72$ (Juniper, Gruffydd-Jones, Ward, & Svensson, 2010)	E	Parent
Independent			
Greenspace—Aims 1 and 3	Continuous: Normalized Difference Vegetation Index (NDVI) Measure of proportion of ground covered by green vegetation (Jackson & Huete, 1991) in each Community Statistical Area (CSA)	N	U.S. geological survey
Neighborhood violent crime rate—Aims 2 and 3	Continuous: Violent crime rate: homicide, rape, aggravated assault, and robbery in Baltimore City that are reported to the Police Department. Incidents are per 1,000 residents in the CSA.	N	Baltimore city police department
Parent perception of neighborhood safety—Aims 2 and 3	Continuous: Subscale of the Perceived Neighborhood Scale (Martinez, Black, & Starr, 2002), (nine questions on a Likert scale). Alpha reliability for this subscale for the study sample = 0.928	E	Parent
Asthma triggers and allergic sensitization			
Allergic sensitization	Dichotomous: Radioallergosorbent test: 5 ml blood. Venipuncture by pediatric emergency department nurse or patient care technician. Test develops allergen sensitization profile	E	Physiologic
Child exposure to secondhand smoke	Dichotomous: 1 ml saliva, collected using sorbettes and swabs. Salivary Cotinine Level (Bernert, McGuffey, Morrison, & Pirkle, 2000; Chang et al., 2000; Hukkanen, Jacob, & Benowitz, 2005; Salimetrics, 2007) <1.0 ng/ml = non to low exposure ≥1.0 ng/ml = positive cotinine	E	Physiologic
Presence of pests in home	Dichotomous: Ask parent if they have seen roaches, rats, or mice in their home in the past three months.	E	Parent
Covariates			
Demographics: Parent age, education, marital status, and race/ethnicity Child age, sex, and race/ethnicity	Baseline Demographic Questionnaire- Age- Continuous, Education- Categorical, Marital Status- Categorical, Sex- Dichotomous, Race/Ethnicity- Categorical	E	Parent
Income	Categorical-Combined Family income (The Regents of the University of California, MacArthur Foundation, 2008)	E	Parent
Season of enrollment	Categorical	E	N/A

This table includes the dependent and independent variables along with potential covariates. The table also describes variable operationalization, whether the data will be added for this study ("New Data") or came from the parent study ("Existing Data") and the informant or source of the data.

TABLE 2 Detectable odd ratios based on predictor distributions and intra-class correlation of asthma control level across community statistical areas

Predictor distribution ^a	Intraclass correlation coefficient		
	0.10	0.15	0.20
10/90	3.58	3.84	4.12
30/70	2.32	2.42	2.53
50/50	2.17	2.26	2.35

^aPotential distribution of high versus low greenspace or high versus low violent crime rate.

3.7 | Data analysis plan

Preliminary analysis will be completed for all study variables to determine if the distribution of the variables meet the assumptions for inferential statistical tests. Variables will be examined for normality and examined with means and standard deviations or medians and interquartile ranges accordingly. If the variables are skewed, statistical approaches that fit the variable distribution (i.e., negative binomial, gamma) will be used if possible. The pattern of missing data will be explored, and t-tests and chi-squared tests will be used to determine if there are differences between those with and without missing data. The significance level will be set at 0.05. All tests will be two-tailed.

Aim 1. Examine the association between neighborhood greenspace and level of asthma control. H1: Lower index of neighborhood greenspace (measured as NDVI) will be associated with poor asthma control.

The primary outcome is level of asthma control defined as either poorly controlled (reference group) or not poorly controlled. The hypothesis will be tested using a multi-level logistic regression model with the child-specific variables in the first level and neighborhood CSA in the second level. The purpose of the analysis is to determine if amount of CSA greenspace is associated with asthma control while controlling for season of enrollment, race/ethnicity, age, sex, indoor asthma triggers, parental education, parent marital status and family income. These covariates will be entered into the model first, followed by greenspace, the independent variable of interest. Individuals will be nested within CSA which will provide robust standard errors. A significant positive coefficient for greenspace will indicate support for the hypothesis.

Aim 2. Examine the associations among neighborhood safety, measured as neighborhood violent crime rate and parent perception of neighborhood safety, and level of asthma control. H2A: Higher rates of neighborhood violent crime will be associated with poor asthma control; H2B: Parent perception of an unsafe neighborhood will be associated with poor asthma control. H2C: Parent perception of neighborhood safety will be more strongly associated with level of asthma control than neighborhood violent crime rate.

The hypotheses will be tested similar to the method for Aim 1 with asthma control as the dichotomous outcome. For hypotheses 2A and 2B neighborhood violent crime rate and parent perception of safety will be examined in separate models including all covariates (season of enrollment, race/ethnicity, age, sex, indoor asthma triggers, parental education, parent marital status and family income). To test hypothesis 2C neighborhood violent crime rate and parent perception of neighborhood

safety will be entered into the model simultaneously to determine the relative contribution of the two variables to asthma control.

Aim 3. Explore neighborhood safety (neighborhood violent crime rate and parent perception of neighborhood safety) as a potential moderator in the association between neighborhood greenspace and level of asthma control. H3: Neighborhood safety will moderate the relationship between greenspace and level of asthma control.

Moderation is considered to occur when the presence of a third variable affects the direction and/or strength of the association between an independent variable and a dependent variable (Baron & Kenny, 1986). Interaction terms will be created for (1) greenspace with neighborhood violent crime rate and (2) greenspace with parent perception of neighborhood safety. Interaction terms will be added to the models described in Aim 2 along with greenspace to test hypothesized moderation. Separate analyses will be conducted for neighborhood violent crime rate and parent perception of neighborhood safety. These moderator analyses are likely to be under powered, therefore, the effect size associated with the interaction will be examined in addition to statistical significance.

4 | DISCUSSION

There are two major innovative aspects of this study. First, multiple methods and informants (geocoding, neighborhood crime statistics, parent reports, and child physiologic measures) will be examined to understand how neighborhood factors are linked to asthma control for predominantly African American, low-income children. Second, the study will be the first to include multiple measures of neighborhood safety, neighborhood violent crime rate and parent perception of neighborhood safety, to better understand its role in modifying the potential benefits of neighborhood greenspace.

One of the benefits of building on an existing database is the ability to maximize the resources that have already been invested to recruit and collect data from a highly vulnerable population of parents and children, without any additional burden to participants (Doolan & Froelicher, 2009). In this study we use the data on asthma control and parent perception of neighborhood safety that was obtained for the original study and add new data on greenspace and neighborhood violent crime rate using publicly available data.

At present, the additional neighborhood data has been added to the existing data set as the final step before data analysis can begin in summer 2018. The challenges of building on existing data are that the methodological approach must include consideration of the available power, data quality and adequacy of the existing data set to answer the research question (Doolan & Froelicher, 2009). The power analysis demonstrated that the study was appropriately powered, given previous research in the area and the variability of asthma control by CSA from the parent study data. We knew that maximizing variability in the neighborhood residences of the study sample would enhance our capacity to address the research question. But as we begin data analysis we are finding limited variability in greenspace and violent crime rate. Perhaps the limited variability is due to economic

segregation that clusters in poverty specific neighborhoods, a problem that has grown tremendously in this country over the last several decades especially among families with children (Owens, 2016). Another potential explanation could be that families living in particular catchment areas are likely to seek care at Johns Hopkins Hospital.

Study participants live across 37 of the 55 CSAs in Baltimore and 77% live in areas with higher poverty than the average in Baltimore City (Baltimore Neighborhood Indicators Alliance- Jacob France Institute, 2015). Research has shown that those living in poverty have less greenspace than those who do not live in poverty (Wen, Zhang, Harris, Holt, & Croft, 2013). Therefore, when average NDVI was calculated for each CSA, the range (0.02, 0.14; SD = 0.035) was not sufficient to analyze the data at this level. To maximize greenspace variability, we revised the definition to include NDVI in circular areas, known as "buffers" in ArcGIS, with radii of 100, 250, 500, and 1,000 m, around each individual's home. Measurement of buffers, a proximal measure of greenspace, has more variability than the administrative unit of CSAs and its validity has been supported (Chen et al., 2017; Sbihi et al., 2015). For example, the NDVI range for the 100m buffer (0.00, 0.20; SD = 0.039) had a slightly higher SD than when measured by CSA. Variability of the violent crime rate across CSAs was also limited (range [7.5, 32.7]; SD = 6.66). To increase variability, violent crime rate was re-analyzed by census tract (range [4.9, 39.6]; SD = 9.17), a smaller administrative unit that captured variability across neighborhoods. This adjustment is congruent with current literature (Beck et al., 2016; Camacho-Rivera, Kawachi, Bennett, & Subramanian, 2014). Although there are challenges related to the use of existing data, thus far, the benefits have outweighed the drawbacks.

4.1 | Limitations

The study limitations are based on study design, measurement of the independent variables, and the study sample. Conclusions about causal relationships among the study variables cannot be inferred based on the cross-sectional nature of the study design. However, we anticipate that the results can be used to guide the development of experimental designs to rigorously test the effect of increasing children's neighborhood greenspace exposure on asthma control, particularly among children growing up in unsafe neighborhoods.

Because this study is building on a parent study there are certain variables that will not be explored fully. For example, we were not able to ask children how much time they spent outside exposed to greenspace. We can only infer that those living in areas with higher greenspace have higher exposure. We have the advantage, however, of being able to add two variables to the data set in order to investigate the phenomena of interest. In addition, the sample size cannot be increased thus the study is not adequately powered to test moderation. Due to this limitation, analysis of aim three will consider effect size, as well as statistical significance, to inform future research.

As with all measurement choices there are limitations and strengths. Violent crime point pattern data contain only information on violent crimes that were reported to police officers, potentially leading to underestimation of the violent crime rate. The potential

underestimation, however, would bias results toward the null. For the purposes of obtaining objective, publicly available data, crime data from police departments is the best option. One limitation of using NDVI to measure greenspace is that this method does not provide information regarding greenspace quality. Due to study design, we were not able to ask parents about the quality of greenspace surrounding their homes. Overall, measuring greenspace using NDVI was efficient and consistent with previous research. In future studies we plan to investigate greenspace quality and exposure.

All of the children in the study sample have persistent asthma, potentially leading to ceiling effects in the outcome variable, level of asthma control. This decreased variability might bias results towards the null. That being said, these children represent those at highest risk for asthma-related morbidity and mortality in that they are predominantly low-income and African American. Therefore, the results of research on asthma control for this population have the potential to make a strong impact. We will be mindful not to generalize our results beyond this population.

5 | CONCLUSION

This study focuses on vulnerable children at high-risk for asthma-related morbidity and mortality. Using multiple methods and informants to investigate modifiable neighborhood factors we will examine how these factors may influence asthma control. The long-term goal of this research is to inform policies and practices for improving health outcomes for children with asthma living in urban poverty by understanding the role greenspace and neighborhood safety might play in asthma control.

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CONFLICTS OF INTEREST

All authors declare no conflicts of interest.

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