Neighborhood Social Conditions, Family Relationships, and Childhood Asthma

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BACKGROUND AND OBJECTIVES: Poor neighborhood conditions have established associations with poorer child health, but little is known about protective factors that mitigate the effects of difficult neighborhood conditions. In this study, we tested if positive family relationships can buffer youth who live in dangerous and/or disorderly neighborhoods from poor asthma outcomes.

abstract

METHODS: A total of 308 youths (aged 9–17) who were physician-diagnosed with asthma and referred from community pediatricians and/or family practitioners participated in this cross-sectional study. Neighborhood conditions around families' home addresses were coded by using Google Street View images. Family relationship quality was determined via youth interviews. Clinical asthma outcomes (asthma symptoms, activity limitations, and forced expiratory volume in 1 second percentile), asthma management behaviors (family response to asthma symptoms and integration of asthma into daily life), and asthma-relevant immunologic processes (lymphocyte T helper 1 and T helper 2 cytokine production and sensitivity to glucocorticoid inhibition) were assessed via questionnaires, interviews, spirometry, and blood draws.

RESULTS: Significant interactions were found between neighborhood conditions and family relationship quality ($\beta = |.11-.15|$; P < .05). When neighborhood danger and/or disorder was low, family relationships were not associated with asthma. When neighborhood danger and/or disorder was high, better family relationship quality was associated with fewer asthma symptoms, fewer activity limitations, and higher forced expiratory volume in 1 second percentile. Similar patterns emerged for asthma management behaviors. With immunologic measures, greater neighborhood danger and/or disorder was associated with greater T helper 1 and T helper 2 cytokine production and reduced glucocorticoid sensitivity.

CONCLUSIONS: When youth live in dangerous and/or disorderly neighborhoods, high family relationship quality can buffer youth from poor asthma outcomes. Although families may not be able to change their neighborhoods, they may nonetheless be able to facilitate better asthma outcomes in their children through strong family relationships.



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Dr Chen conceptualized and designed the study, conducted data analyses, and drafted the initial manuscript; Drs Miller, Shalowitz, and Story conceptualized and designed the study and reviewed and revised the manuscript; Ms Hayen and Ms Le coordinated and supervised data collection, contributed to the acquisition of data, and reviewed and revised the manuscript; and Ms Austin contributed to the acquisition of data and data interpretation and reviewed and revised the manuscript.

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WHAT'S KNOWN ON THIS SUBJECT: Neighborhood conditions have established associations with childhood asthma, but little is known about the protective factors that can help buffer the effects of poor neighborhood social environments on childhood asthma.

WHAT THIS STUDY ADDS: Under conditions of high neighborhood danger and/or disorder, good family relationships were associated with fewer asthma symptoms, fewer activity limitations, and better pulmonary functioning. Because neighborhoods are difficult to change, 1 route to improving asthma outcomes may be through family relationships.

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The characteristics of a neighborhood (both physical and social) can influence the health of those who live in that neighborhood.^{1,2} With respect to social conditions, living in neighborhoods with high residential segregation and economic deprivation increases the risk of adverse health outcomes, including cardiovascular disease and overall mortality.^{3,4} Neighborhood violence also increases the risk of asthma, obesity, and coronary heart disease.^{5–8}

Despite these risks, there are often obstacles that prevent families from moving away from undesirable neighborhoods. As a result, they must find ways to adapt to the stressors their neighborhoods present. Little is known about factors that facilitate such adaptation. Psychosocially, supportive family relationships may be 1 such buffer, protecting individuals from cardiometabolic risks associated with other childhood adversities (eg, low socioeconomic status, divorce, and abuse).9-11 Here. we tested if supportive family relationships serve a similar buffering function in the context of childhood asthma.

Asthma is the most prevalent chronic condition in childhood, imposes a substantial economic burden on the country, and is associated with impairment in multiple domains of functioning.¹² Asthma incidence is higher in neighborhoods with adverse conditions (those with high violence and disorder), and these conditions are also associated with worse asthma control.^{13,14} We hypothesized that family relationships would interact with neighborhood danger and/or disorder to predict clinical outcomes (symptoms, activity limitations, and pulmonary functioning) in a sample of children with asthma. We hypothesized 2 reasons for such effects. Hypothesis 1 was that positive family relationships help youth maintain good asthma management behaviors in the face of

difficult neighborhood conditions. Hypothesis 2 was that positive family relationships buffer the effects of neighborhood conditions on biological processes implicated in stress and asthma.¹ Asthma is a disease characterized by inflammation, constriction, and hypersensitivity of the airways. T helper lymphocytes are key drivers of the pathology that initiates and maintains these processes, and excessive production of T helper 1 (Th1) and T helper 2 (Th2) cytokines¹⁵ released by these lymphocytes are thought to be involved in multiple aspects of asthma pathology.^{15–17} In addition, glucocorticoids play a major role in the physiology and treatment of asthma. Pharmacologic doses of glucocorticoids inhibit Th1 and Th2 cytokine production; however, there is individual variability in sensitivity to these agents.¹⁸ We thus tested interactions of neighborhood by family characteristics on asthma management behaviors (family responses to symptoms and integration of asthma into daily life) and on asthma-relevant immune processes (Th1 and Th2 cytokine responses to ex vivo stimulation and the sensitivity of these responses to inhibition by glucocorticoids).

We used a novel approach to investigate neighborhood social conditions. Authors of many previous studies have relied on census-level variables or questionnaires to characterize neighborhoods. Census data capture broad structural aspects of neighborhoods (eg, percentage of people living below poverty) but not information about day-to-day experiences in neighborhoods.¹⁹ Questionnaires are by nature subjective. Recent technological advances allow researchers to circumvent these problems and perform systematic observations by taking a "virtual walk" with Google Street View to objectively characterize neighborhoods (in terms of the presence of graffiti or deteriorated buildings, for example).^{19,20}

We hypothesized that when youth with asthma live in more dangerous and disorderly neighborhoods, having supportive family relationships would be associated with fewer asthma symptoms and activity limitations and better pulmonary function. In contrast, when youth live in less dangerous and/or disorderly neighborhoods, family relationships would not be associated with asthma outcomes. We hypothesized that similar interaction effects would be found for asthma management behaviors and asthma-relevant immune processes.

METHODS

Participants

A total of 308 youths aged 9 to 17 years old who were diagnosed with asthma by a physician were recruited from the Chicagoland area between 2013 and 2016 through NorthShore University Health System and Erie Family Health Center, via referrals from community pediatricians and family practitioners. All patients had a current diagnosis of asthma and had seen a physician for asthma within the past 24 months. Inclusion criteria were fluency in English and no acute respiratory illness at the visit. Exclusion criteria were other chronic physical illnesses. Youth gave written assent, and parents provided written consent. This study was approved by the Northwestern, NorthShore, and Erie Institutional Review Boards.

Procedures

Participants completed interviews, questionnaires, spirometry, and a venous blood draw. Parents and youth were each compensated \$80.

Measures

See the Supplemental Information for additional details.

Neighborhood Characteristics via Google Street View

Trained raters completed virtual walks through identified street segments using Google Earth Pro and Google Street View imagery and systematic social observation methods developed by Odgers et al.¹⁹ Virtual walks involved detailed inspection of streets, sidewalks, signage, and all buildings and adjacent yards or land. Neighborhood characteristics recorded during virtual walks included signs of physical disorder (litter, run-down cars, small graffiti, large graffiti, scrubbed or painted-over graffiti, or other defaced property) and raters' global assessment of neighborhood dangerousness (based on the presence of abandoned and/or boarded-up homes, vacant lots, bars on windows and/or doors, and police cameras; in addition, the presence of institutions such as churches or schools were considered mitigating factors). Interrater reliability for the 2 scales ranged from 0.77 to 0.90. Because of their high correlation (r = 0.65; P < .001), the dangerousness and disorder scales were standardized and averaged to create a single neighborhood danger and/or disorder score.

Family Relationship Quality

Family relationship quality was determined via interviews with youth using the University of California Los Angeles Life Stress Interview.^{21,22} This interview is used to probe trust, support, and conflict in youth's relationships with family members. Higher numbers reflected betterquality family relationships.

Asthma Clinical Outcomes

Pulmonary function was assessed in the laboratory by using spirometry (MicroLoop; CareFusion, San Diego, CA) according to American Thoracic Society guidelines.²³ Forced expiratory volume in 1 second (FEV₁) percentile was calculated on the basis

of child age, sex, ethnicity, and height.²⁴

Asthma activity limitations were measured by child report by using the Activity Limitations subscale of the Pediatric Asthma Quality of Life Questionnaire.²⁵ Higher scores indicate greater activity limitations.

Parent report of child asthma symptoms was queried with an item question for parents: "How often has your child had a cough, wheeze, shortness of breath, or chest tightness during the past month?"²⁶ Higher numbers indicated more asthma symptoms.

Asthma Management Behaviors

The Family Asthma Management System Scale (FAMSS)²⁷ is a semistructured interview that is used to query how families respond when they perceive breathing problems in the child (family response to symptoms and child response to symptoms) as well as how well families balance managing asthma within their daily lives (balanced integration of asthma). Higher scores indicate better responses to symptoms and better balanced integration.

Asthma Immunologic Measures

Th1 and Th2 cytokine production were measured by ex vivo stimulated peripheral blood mononuclear cells (PBMCs). A total of 0.5 imes 10⁶ PBMCs were isolated from venous blood by density-gradient centrifugation and incubated with 25 ng/mL of phorbol 12-myristate 13-acetate (PMA) and $1 \,\mu\text{g/mL}$ of ionomycin for 24 hours at 37° C in 5% CO₂.^{28–30} After incubation, supernatants were harvested and assayed in duplicate via electrochemiluminescence on a Sector Imager 2400A (Meso Scale Discovery, Rockville, MD)³¹ for Th2 (interleukin 4, interleukin 5, interleukin 10, and interleukin 13) and Th1 (interferon- γ , interleukin 2) cytokines. Composite Th1 and Th2 scores were derived by standardizing each cytokine and then averaging values as described by Ehrlich et al.³²

Glucocorticoid sensitivity was measured by repeating the above protocol, this time with 1.38×10^{-6} M hydrocortisone added.^{33,34} At this dose, cortisol suppresses production of Th1 and Th2 cytokines, so higher values reflect greater insensitivity to glucocorticoid inhibition.

Covariates

The covariates included child sex, age, ethnicity (white versus nonwhite), family income, asthma severity (based on the higher of symptom frequency and medication use²⁶), and whether the child was using an inhaled corticosteroid (yes or no) and a β -agonist (yes or no for short acting or long acting).

Statistical Analyses

We conducted hierarchical multipleregression analyses according to Aiken and West,³⁵ in which asthma outcomes were predicted from (1) covariates described above, (2) main effects of neighborhood conditions (danger and/or disorder score) and family relationship quality (life stress interview family relationship score), and (3) the interaction between neighborhood conditions and family relationships. Positive interaction coefficients mean that at high levels of 1 variable, there is a positive association between the second variable and the outcome variable. Coefficients are presented as standardized β coefficients, which can be interpreted in terms of SD units; for example, a coefficient of .2 would indicate that for every 1 SD increase in the independent variable, the dependent variable increases by 0.2 SDs. Predictor variables were centered before analyses. Because neighborhood conditions and family relationships are continuous variables, figures were created with estimated regression lines plotted at ± 1 SD of these variables.

TABLE 1 Sample Characteristics

	Mean	SD	%
Child age, y	12.99	2.50	_
Sex			
Male	_	_	55
Child ethnicity			
White	—	—	50
African American	—	—	26
Hispanic	—	—	14
Asian American	—	—	10
Family income	6.35	2.07	
β-Agonist	—	—	97
Inhaled corticosteroid	—	—	72
Asthma severity			
Mild intermittent	—	—	16
Mild persistent	—	—	43
Moderate	—	—	27
Severe	—	—	14
Family relationship quality	2.06	0.79	
FEV ₁ , %	94.95	15.24	
Activity limitations	3.34	1.30	
Parent-reported asthma symptoms	1.31	0.59	
Asthma management			
Family response	5.95	1.96	—
Child response	4.75	2.04	_
Balanced integration	5.54	1.68	

Family income ranges from 1 to 9. The mean of 6.35 corresponds to the \$75 000-\$99 999 category. β -Agonist refers to long acting or short acting. Asthma severity ranges from 1 to 4. Family relationship quality ranges from 1 to 5. Activity limitations range from 1 to 7. Parent-reported symptoms ranges from 1 to 4. Asthma management behaviors range from 1 to 9. Values are not included for neighborhood danger and cytokine composites because they all have a mean of 0 and an SD close to 1 (given how scoring was done). —, not applicable.

RESULTS

Table 1 presents information about sample characteristics. Detailed results are in Tables 2 through 4.

Main Effects of Family Relationship Quality

Asthma Clinical Outcomes

There were no main effects of family relationship quality on asthma clinical outcomes.

Asthma Management Behaviors

Higher-quality family relationships were associated with better family responses to asthma symptoms ($\beta = .18$; P = .002) and also with better balanced integration of asthma into daily life ($\beta = .24$; P < .001).

Immunologic Measures

Family relationship quality was not related to immunologic measures.

Main Effects of Neighborhood Danger and/or Disorder

Asthma Clinical Outcomes

Higher neighborhood danger and/or disorder was associated with greater asthma-related activity limitations ($\beta = .18$; P = .004).

Asthma Management Behaviors

Greater neighborhood danger and/or disorder was associated with poorer family responses to asthma symptoms ($\beta = -.14$; P = .027).

Immunologic Measures

Greater neighborhood danger and/or disorder was associated with larger Th2 cytokine responses to PMAionomycin stimulation ($\beta = .16$; P = .025) and with larger Th1 cytokine responses ($\beta = .14$; P = .049).

Greater neighborhood danger and/or disorder also was associated with less sensitivity to glucocorticoids' inhibitory properties (ie, more Th2 cytokine production despite the addition of cortisol; $\beta = .16$; P = .026). The main effect of neighborhood danger and/or disorder for Th1 cytokine production with cortisol was $\beta = .13$; P = .08.

Interaction Effects: Family Relationships \times Neighborhood Danger and/or Disorder

Asthma Clinical Outcomes:Activity Limitations

There was a significant interaction between family relationship quality and neighborhood conditions ($\beta = -.10$; P = .048). Figure 1 reveals that at lower levels of neighborhood

 TABLE 2 Regression Analyses of Neighborhood Danger and Family Relationship Quality Predicting Asthma Outcomes

	Child-Reported Activity	Parent-Reported Asthma	FEV ₁ %,
	Limitations, B	Symptoms, B	β
Step 1			
Age	053	091	.059
Sex	—.171 ^{***}	066	076
Ethnicity	171**	039	.106
Income	.033	.004	061
Asthma severity	.209**	.523***	056
β-Agonist	003	.003	027
ICS	188***	213****	081
Step 2			
Neighborhood danger	.180***	047	038
Family relationship quality	105	027	.025
Step 3			
Neighborhood danger $ imes$ family relationship	—.109 [*]	125 [*]	.129*

ICS, inhaled corticosteroid.

* P < .05.

** *P* < .01.

*** P < .001.

danger and/or disorder, activity limitations are low and do not vary by family relationship quality ($\beta = .01$; P = .94). At higher levels of neighborhood danger and/or disorder, the higher the family relationship quality, the fewer activity limitations a child experiences ($\beta = -.20$; P = .008).

Asthma Clinical Outcomes: Parent Report of Asthma Symptoms

A significant interaction between neighborhood conditions and family relationship quality ($\beta = -.12$; P =.016) indicated that at lower levels of neighborhood danger and/or disorder, parent-reported symptoms do not vary by family relationship quality ($\beta = .10$; P = .19). At higher levels of neighborhood danger and/or disorder, the higher the family relationship quality, the fewer parentreported symptoms a child has ($\beta =$ -.13; P = .046).

Asthma Clinical Outcomes: Spirometry

A significant interaction effect (β = .13; *P* = .027) indicated that at lower levels of neighborhood danger and/or disorder, FEV₁ does not vary by family relationship quality (β = -.11; *P* = .21). At higher levels of neighborhood danger and/or disorder, the association between family relationship quality and FEV₁ was β = .13; *P* = .07.

Asthma Management Behaviors: Family Response

There was a significant interaction effect for family response to asthma symptoms ($\beta = .13$; P = .025). Figure 2 reveals that at lower levels of neighborhood danger and/or disorder, family response to asthma symptoms is good and does not vary by family relationship quality ($\beta = .06$; P = .49). At higher levels of neighborhood danger and/or disorder, the higher the family

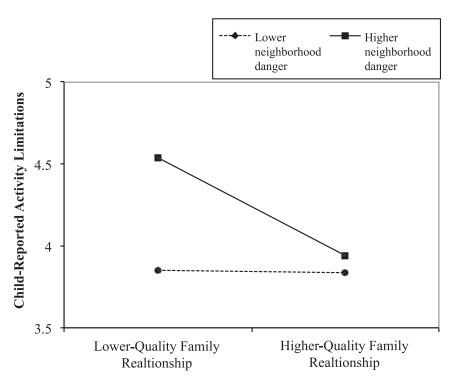


FIGURE 1

Interaction between neighborhood conditions and family relationship quality predicting asthma activity limitations, with higher scores indicating more activity limitations. The figure depicts estimated regression lines at ± 1 SD of neighborhood danger. Lower and higher family relationship quality also refer to ± 1 SD.

relationship quality, the better a family's response to asthma symptoms ($\beta = .29$; P < .001).

Asthma Management Behaviors: Child Response

A significant interaction effect ($\beta = .11$; P = .05) revealed that at lower levels of neighborhood danger and/or disorder, child response to asthma symptoms does not vary by family relationship quality ($\beta = -.03$; P = .74). At higher levels of neighborhood danger and/or disorder, the higher the family relationship quality, the better a child's response to symptoms ($\beta = .18$; P = .02).

Asthma Management Behaviors: Balanced Integration

There was an interaction effect for balanced integration ($\beta = .15$; P = .006). Figure 2 reveals that at lower levels of neighborhood danger and/or disorder, balanced integration does not vary by family relationship quality ($\beta = .09$; P = .26). At higher levels of neighborhood danger and/or disorder, the higher the family relationship quality, the more balanced integration a family has ($\beta = .36$; P < .001).

Asthma Management Behaviors: Immunologic Measures

There were no interaction effects between family relationship quality and neighborhood conditions for immunologic measures.

DISCUSSION

The current study is the first that we are aware of to leverage Google Street View technology to better understand variations in children's asthma outcomes. Using systematic observations, we found that danger and disorder in children's neighborhoods was associated with worse asthma outcomes across multiple indicators. Additionally, we found evidence suggesting that positive family relationships may override these effects. Specifically,

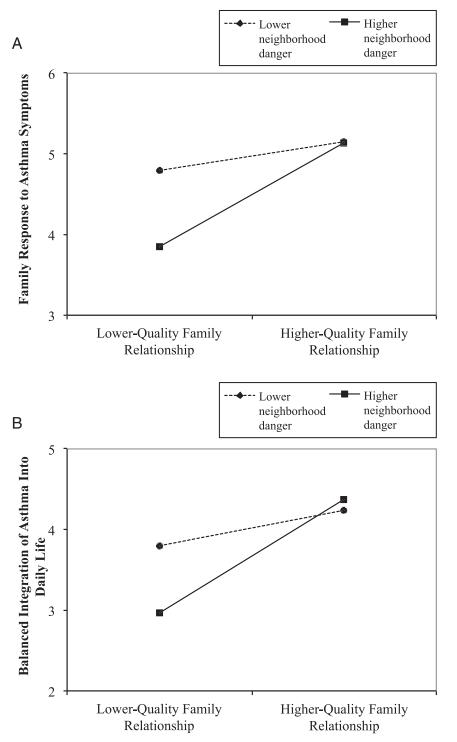


FIGURE 2

Interaction between neighborhood conditions and family relationship quality predicting asthma management behaviors. A, How well families respond to their child's asthma symptoms. B, How well families balance managing asthma within their daily lives. In both cases, higher scores indicate better asthma management. The figure depicts estimated regression lines at ± 1 SD of neighborhood danger. Lower and higher family relationship quality also refer to ± 1 SD.

when neighborhood danger and/or disorder is high, having higher-quality family relationships is associated with fewer parent-reported asthma symptoms, fewer asthma activity limitations, and better pulmonary functioning. Youth exposed to high neighborhood danger and/or disorder but with high-quality family relationships had asthma profiles similar to youth in low danger and/or disorder neighborhoods.

These findings are consistent with previous research that has documented links between neighborhood violence and asthma,^{5,13,14} and research that has documented associations between neighborhood danger and other health outcomes such as obesity and depression.³⁶⁻³⁹ In the current study, we advance previous research in 2 ways. First, we move beyond the main effects of neighborhoods to examining protective factors. The 1 previous study in which Google Street View images were used revealed the main effects of neighborhood disorder and danger on children's antisocial behaviors.¹⁹ Here, we extend those findings to a physical health outcome and find evidence that positive family relationships buffer youth from the health risks associated with neighborhood danger and/or disorder. This finding is consistent with other research on family relationships as stress buffers against health problems^{9-11,40-42} but extends that work to neighborhood conditions.

The second advance is showcasing the utility of a new methodology for neighborhood and health research. Authors of many previous studies relied on participant reports of neighborhood characteristics, which are open to subjective biases. In the current study, we address this by having coders rate neighborhood conditions. What makes this possible to do is the wealth of images available through Google Street View, whereby a coder can take a walk through a person's neighborhood virtually. This eliminates the expense of having to send raters driving through the neighborhoods of participants.²⁰ In addition, it is a more meaningful

 TABLE 3 Regression Analyses of Neighborhood Danger and Family Relationship Quality Predicting Asthma Management Behaviors

	Family Response to	Child Response to	Integration of
	Asthma Symptoms, β	Asthma Symptoms, $\boldsymbol{\beta}$	Asthma Management Into Daily Life, β
Step 1			
Age	157**	040	005
Sex	079	162**	.152**
Ethnicity	051	.015	.197**
Income	.091	.120*	.087
Asthma severity	014	061	232 ^{****}
β-Agonist	.100	.148*	.059
ICS	.066	.065	.156*
Step 2			
Neighborhood danger	142 [*]	102	112
Family relationship quality	.185**	.084	.235***
Step 3			
Neighborhood danger $ imes$ family relationship	.127*	.110	.147**

ICS, inhaled corticosteroid.

** *P* < .01.

*** P < .001.

indicator of neighborhoods than census variables. There are struggles with census data in terms of accurately defining what represents a neighborhood to an individual and in terms of census variables not always reflecting people's lived experiences in a neighborhood. In contrast, Google Street View coding is focused on a narrowly defined, precise area that reveals where participants walk and what they see in their daily lives.

Through what processes would positive family relationships buffer children from the effects of dangerous or disorderly neighborhoods? One explanation is that when families live in difficult neighborhoods, positive family relationships may mean that parents are making efforts to shield

 TABLE 4 Regression Analyses of Neighborhood Danger and Family Relationship Quality Predicting Asthma-Relevant Immunologic Outcomes

	PMA-lonomycin	PMA-lonomycin	PMA-lonomycin	PMA-lonomycin
	Th1 Cytokines, β	Th2 Cytokines, β	and Cortisol Th1	and Cortisol Th2
			Cytokines, β	Cytokines, β
Step 1				
Age	130 [*]	.112	060	.087
Sex	021	.042	004	027
Ethnicity	118	161*	096	127
Income	.002	.052	.056	.069
Asthma severity	034	005	053	004
β-Agonist	005	006	015	010
ICS	.035	020	.098	.034
Step 2				
Neighborhood danger	.139*	.158*	.128	.163*
Family relationship quality	012	056	060	016
Step 3				
Neighborhood danger $ imes$ family relationship	.042	036	.027	—.056

PMA-ionomycin is the incubation of PBMCs with 25 ng/mL of phorbol 12-myristate 13-acetate \pm 1 μ g/mL of ionomycin. ICS, inhaled corticosteroid.

* P < .05.

their children by not allowing the neighborhood environment to disrupt family life and routines. For children with asthma, this may mean that parents prioritize asthma management and teach their children how to stay focused on maintaining their health (eg, being aware of symptoms and responding to them in a timely manner), regardless of what is going on in their neighborhood.

In contrast, it did not appear that positive family relationships buffered physiologic responses to stress because there were no interactions predicting cytokine production. Rather, there were direct effects of neighborhoods, such that worse conditions were associated with larger Th1 and Th2 responses to mitogenic stimulation and lower glucocorticoid sensitivity of Th2 cytokines. These patterns suggest that neighborhood social characteristics may function as another level of stressor linked to biological processes in asthma, similar to stressors at the individual and family levels.^{33,43–47} It is possible that biological responses to neighborhood stressors may be buffered by individual-level characteristics such as coping^{48,49} or functional connectivity of brain networks involved in selfregulation.50

Strengths of the current study include the systematic social observation of neighborhoods using Google Street View, the interview-based measures of family relationships and asthma management (considered gold standards), and the battery of immune processes assessed in youth. Limitations include the fact that causality cannot be determined from observational data and the crosssectional nature of this study design. In addition, Google Street View images provide a 1-time snapshot that may not accurately capture a neighborhood over time, and we were limited by only having current family addresses.

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^{*} P < .05.

Implications of this study include the idea that if families have to live in dangerous and/or difficult neighborhoods, there may be options for minimizing the effects of neighborhood conditions on their child's asthma. In particular, strong family relationships may help promote better asthma outcomes in youth perhaps because high-quality relationships help youth figure out how to manage their asthma despite neighborhood stressors. In future studies, the efficacy of family interventions among youth with asthma who live in high-danger neighborhoods could be tested. These types of interventions have been found to improve inflammatory cytokine profiles,⁵¹ cortisol levels,⁵² and outcomes in youth with diabetes,^{53,54} so they might be

beneficial among youth with asthma as well. These types of interventions also have the strongest effects on those who are at highest risk at program entry,^{55–58} so they might be particularly useful if targeted at youth living in difficult neighborhoods.

CONCLUSIONS

In the current study, we demonstrated that when neighborhoods are characterized as dangerous and disorderly, betterquality family relationships are associated with better asthma management behaviors and better asthma outcomes. These patterns are apparent across multiple clinical indicators, including symptoms, activity limitations, and lung function. Together, the results suggest that although families may not be able to do much to change the neighborhoods in which they live, they may nonetheless be able to facilitate better asthma outcomes in their children through strong family relationships.

ABBREVIATIONS

FAMSS: Family Asthma Management System Scale
FEV₁: forced expiratory volume in 1 second
PBMC: peripheral blood mononuclear cell
PMA: phorbol 12-myristate 13acetate
Th1: T helper 1
Th2: T helper 2

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