RELATIONSHIPS BETWEEN COMMUNITY VIOLENCE AND SENSITIZATION AND EXPOSURE TO COCKROACH ALLERGEN AMONG ASTHMATIC INNER-CITY CHILDREN

Michelle L. Sever, MSPH

A dissertation submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Department of Epidemiology.

Chapel Hill
2012

Approved By:

James C. Thomas, PhD

Julie Daniels, PhD

Karin B. Yeatts, PhD

Mike Emch, PhD

Darryl Zeldin, MD

Abstract

MICHELLE L. SEVER: Relationships between Community Violence and Sensitization and Exposure to Cockroach Allergen among Asthmatic, Inner-City Children
(Under the direction of James C. Thomas, MPH, PhD)

Background: Asthma, a chronic respiratory disease which affects more than 10 million children in the United States, disproportionately affects minority and socioeconomically disadvantaged children. The Inner City Asthma Study (ICAS) was one of the first multicenter intervention trials intended to reduce allergen exposure and subsequent asthma morbidity among inner-city children. The intervention was successful in reducing both cockroach allergen exposure and asthma morbidity. In ICAS, children exposed to high levels of violence in their neighborhood had higher asthma morbidity at baseline, even after controlling for other risk factors. The relationship between violence exposure and asthma morbidity is thought to be mediated by either the physiologic response to violence or by increased exposure to indoor allergens due to increased time spent indoors because of violence in the neighborhood. Methods: We examined whether the relationship between community violence and asthma morbidity differed by allergen exposure and sensitization status, and whether crime data could be used as a surrogate for respondents' perceptions of community violence assessed by questionnaire. We used linear mixed models to determine if the effect of the ICAS intervention varied with community violence exposure and allergy to cockroaches. Results: Violence and

cockroach exposure/sensitization were found to interact: children exposed to high levels of community violence had more asthma symptom days, but only if they were also exposed and sensitized to cockroach allergen (pinteraction = 0.07). The same trend was observed with crime data when evaluating the number of assaults per census tract (p=0.14), but not when evaluating census tract assault rate (p=0.22). Children sensitized to cockroach allergen with the highest violence exposure had the greatest reduction in asthma morbidity following a decrease in cockroach allergen exposure in their bedroom. The children not sensitized to cockroach allergen also had a decrease in their asthma symptom days but the decrease in symptom days did not vary by level of violence exposure. Conclusions: These findings support the hypothesis that higher asthma morbidity seen in children exposed to violence in their neighborhoods is due, at least in part, to them spending more time indoors leading to higher exposure to indoor allergens, specifically cockroach allergen.

I dedicate my dissertation to all those who will come behind me, who have seen my hard work and dedication, as well as my faults and flaws, and will be inspired to accomplish something they weren't sure was possible.

O love the LORD, all ye his saints: for the LORD preserveth the faithful, and plentifully rewardeth the proud doer. Be of good courage, and he shall strengthen your heart, all ye that hope in the LORD. Psalm 31:23-24

This work is also dedicated to the memory of my uncle, Dr. Raymond J. Sever, the original Dr. Sever. He always inspired and encouraged me to pursue my PhD and passed away before seeing it come to pass following a valiant battle with pancreatic cancer. He is greatly missed.

Acknowledgments

I must first give thanks to my Lord and Savior Jesus Christ, the indwelling Holy Spirit and my Father in heaven, without whom this would not have been possible. It is only by the grace and mercy of God that I have been able to complete this journey. The support, love, prayers and encouragement of my family at Cup of Salvation Deliverance Church & Ministries was absolutely invaluable. Thank you for believing in me and holding me accountable to complete my PhD. To my pastor, mentor, friend and father, Apostle Dr. Johnny Holloway, I will never be able to express how much you mean to me. Your unconditional love has kept me going through the tough times. Thank you for helping me see myself through God's eyes. To my parents, Tom and Lennie Sever, thank you for giving me space to do what God called me to do without too many guilt trips for neglecting you (smile). I appreciate all your support and love.

Thank you to all my committee members for putting up with me. A special thanks to Jim Thomas for agreeing to chair my committee when it seemed like there was no one really interested in the work I wanted to do. Your guidance and support have been invaluable to me. I must also thank Dr. Darryl Zeldin and the NIEHS for supporting me through grad school and allowing me enough flexibility in my

schedule that I could work and go to school full-time. I greatly appreciate all the opportunities that I have been given.

I must also thank all the folks at Rho, Inc. that helped me through this process, guided me through SAS problems and gave of themselves to help me complete my research. I am grateful to have worked with Agustin Calatroni, Cindy Visness, Tee Bahnson, Ben Vaughn, Herman Mitchell and Sam Arbes among others. I am really looking forward to working with you all on an on-going basis when I start my new job at Rho in a few weeks.

Lastly, I would be remiss not to thank my fellow members of E-PHI!! Ahinee, Eboni, Keisha and Joseph, you have all been my rock over these past six years. Ahinee, I could not have asked for a more faithful and encouraging dissertation partner. I will never look at Panera Bread the same way. Love you guys!

Table of Contents

List of Tables

List of Figures

List of Abbreviations

ANOVA	Analysis of Variance
ETS	Environmental Tobacco Smoke
GIS	Geographic Information System
ICAS	Inner-City Asthma Study
NCICAS	National Cooperative Inner-City Asthma Study
NIAID	National Institute of Allergy and Infectious Diseases
NIEHS	National Institute of Environmental Health Sciences
NIH	National Institutes of Health
NSLAH	National Survey of Lead and Allergens in Housing
SPT	Skin Prick Testing

Chapter 1: Introduction & Background

Asthma in the United States

Asthma is a chronic respiratory disease characterized by attacks of wheezing, shortness of breath, chest tightness, and coughing. It is not fully understood why some people develop asthma and others do not; however, it is generally accepted that asthma is the result of the interaction between genetic susceptibility and environmental exposures, such as indoor allergens and air pollution.[1] Numerous studies have shown that individuals with asthma are more likely to be sensitized to at least one indoor allergen than individuals who do not have asthma.[2]

Asthma is a complex disease of high public health importance. Based on 2008 US data from the National Health Interview Survey, asthma affects more than 10 million children (13.8%) 18 years of age or younger, and disproportionately affects minority (21.1% Black vs. 13% White) and socioeconomically disadvantaged (17% low income vs. 12.6% average income) children.[3] In adults, 16.4 million (7.3%) have current asthma, including 7.2% of whites, 8.1% of blacks and 5.6% and 7.6% of Hispanics and Non-Hispanics, respectively.[4] When further considering race and ethnicity, Puerto Rican children have a higher current asthma prevalence rate than other Hispanic groups (17% vs. 6.2%) and a current asthma prevalence rate 125% higher than non-Hispanic whites and 80% higher than non-Hispanic blacks.[5]

In 2006, asthma accounted for 10.6 million visits to office-based physicians, 6.4 million hospital outpatient visits, 0.4 million discharges from short-stay hospital visits, and 0.2 million hospitalizations.[6-8] The economic cost of asthma in the U.S. in 2010 was estimated to be $20.7 billion.[9] The National Center for Health Statistics found in data collected from 2005 to 2007 that while current asthma prevalence and lifetime diagnosis of asthma are similar for blacks and whites, 9.4% vs. 7.5% and 13.0% vs. 11.2%, respectively, blacks are five times as likely to visit the emergency room for asthma and more than three times as likely to be hospitalized or to die from asthma than whites.[8,10]

The reasons for childhood asthma disparities are multi-faceted and involve genetic, community (healthcare access, inadequate health insurance, violence, sedentary lifestyles, family and social structure) and environmental (indoor and outdoor air pollution, allergens, environmental tobacco smoke) factors. One of the most important environmental exposures associated with asthma and allergic disease is exposure to indoor allergens, such as those from dust mites, cats, dogs, cockroaches, rodents, and molds.[11-18]

Indoor Allergen Sensitization and Exposure

Exposure and sensitization to many indoor allergens is very common, particularly in inner-city environments. 94% of children screened for the multi-site Inner City Asthma Study (ICAS) were sensitized to at least one indoor allergen; however, the prevalence of sensitization to each allergen varied across study sites.[19] For example, 81% of children enrolled in the Bronx were sensitized to cockroach allergen compared to 44% in Seattle. Many of these children were sensitized to

more than one allergen included in the skin test panel (cat, dog, dust mite, cockroach, mouse, rat and mold) which is not uncommon.[20] Nationally, prevalence of sensitization to indoor allergens has been estimated at 42-54% irrespective of asthma status. Among those with asthma, the prevalence of sensitization is much higher with estimates ranging from 62-79%. Sensitization rates differ marginally across age groups, but are generally higher in children and young adults than in adults middle-aged and older.[20,21]

Allergen sensitization is typically correlated with allergen exposure. In ICAS the patterns of exposure to dust mite and cockroach allergens was very similar to that of sensitization to those allergens.[19] Nationally, exposure to indoor allergens is more prevalent than might be expected. More than 40% of homes in the National Survey of Lead and Allergens in Housing (NSLAH) had detectable levels of cockroach allergen with 13% having concentrations above the proposed sensitization threshold of 2 U/g dust.[22] Cockroach allergen exposure was more common in urban areas and high rise buildings and in low income homes. Exposure to mouse allergen at both the levels for detection and sensitization was common nationally at 82% and 22%, respectively and was also more frequent in urban areas and in low income homes.[2] In the NSLAH cat and dog allergen were detected in >99% of homes and dust mite allergen was found in 82% of homes.[2,23,24]

Indoor Allergens and Asthma

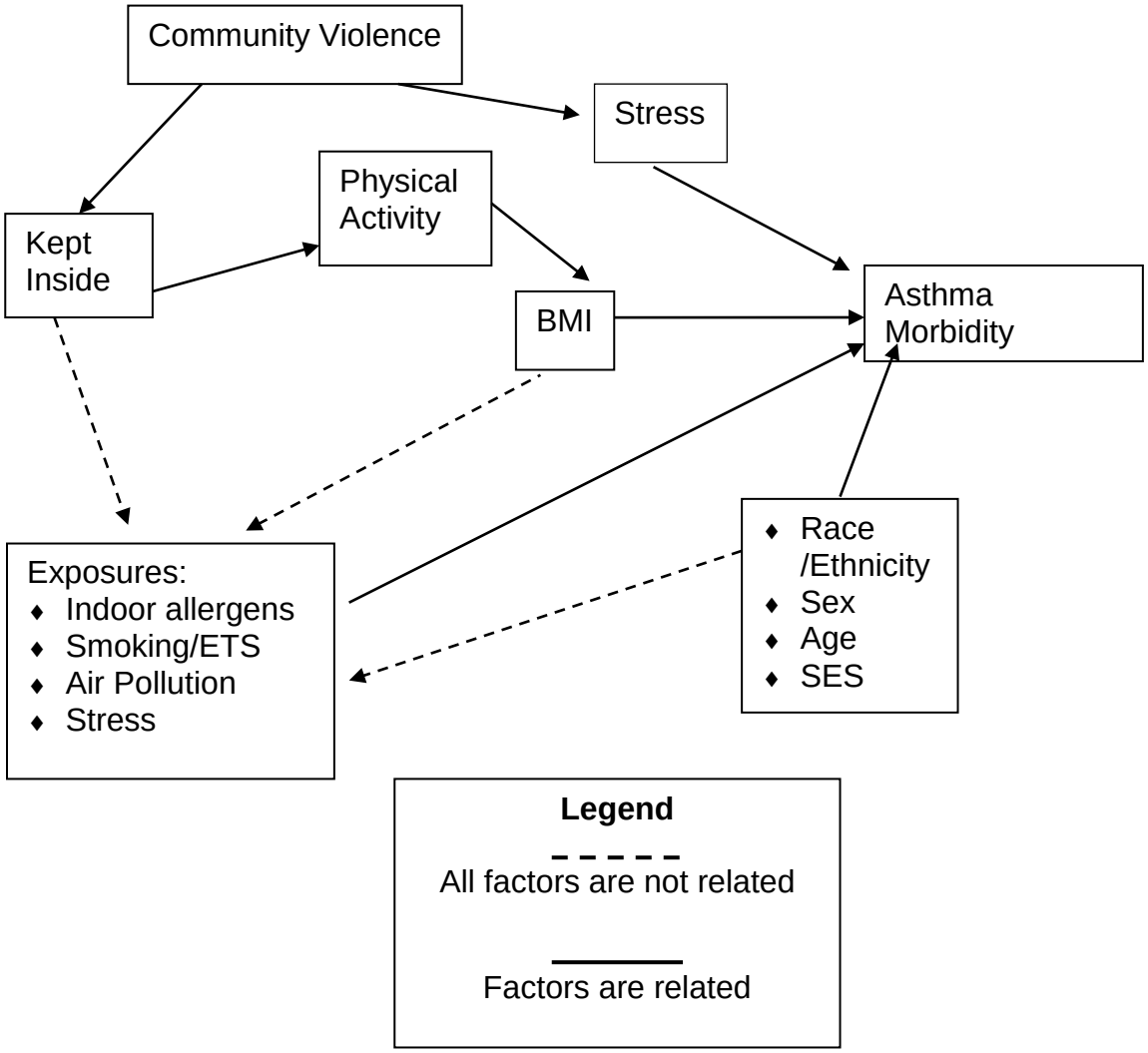
Early exposure to dust mite allergen is associated with increased risk of asthma,[25] and sensitization to cockroach allergen has been widely shown to be associated with asthma.[12,26-31] Sensitization to indoor allergens is related to airway

hyperresponsivesness and wheezing,[32,33] and approximately 80% of school-age children with asthma are allergic to at least one common environmental allergen.[29,34] Findings from several studies suggest a causal relationship between allergen exposure and the development of asthma.[12,18]

Studies have also clearly shown that exposure can lead to both acute and chronic symptoms in sensitized asthmatics.[12,18,19,34,35] Seasonal allergens are triggers of asthma; however, exposure to indoor allergens may be greater given the substantial amount of time spent indoors as well as the year-round exposure to many indoor allergens. Urban populations are becoming more frequently sensitized to indoor allergens (e.g., cockroach) and less frequently sensitized to pollens and outdoor allergens.[36,37] Inner-city children with asthma are more likely to be sensitive to indoor allergens than outdoor allergens, emphasizing the importance of indoor allergen exposure in this population.[38,39] In the National Cooperative Inner-City Asthma Study (NCICAS), more than half the households had high levels (>8 U/g dust) of cockroach allergen with more than a third of the children sensitized to cockroach allergen.[34] Children in NCICAS who were both sensitized and highly exposed to cockroach allergen were 3.4 times as likely to be hospitalized for asthma, had 78% more unscheduled visits to a medical care provider and had more days of wheezing. Most of the children in ICAS were exposed to levels of allergens in their homes believed to be associated with allergic sensitization and disease.[40]

Conceptual Framework

Figure 1. Conceptual framework for the relationships between aggregate and individual factors and asthma morbidity.



Community Violence Exposure and Health Effects

Community violence is exposure to violence at the neighborhood level that may or may not be directed toward the respondent and is not inclusive of exposure to violence in the home. National estimates of childhood exposure to community violence range from 24.8 to 29.7%.[41] Community violence has been linked to increased asthma incidence and morbidity in inner-city children[42-44] and adults;[45] however, children in two cities in Puerto Rico showed no association between exposure to community violence and asthma.[46] Wheezing in early life has been associated with exposure to violence,[42,44] and exposure to violence may also modify the relationship between traffic-related air pollution and asthma in children.[47]

Community Violence and Stress

Community violence is also related to stress and other mental health outcomes. Children exposed to chronic community violence were more anxious and fearful, played more aggressively, and had increased neurocognitive deficits. High crime rates have also been linked to negative birth outcomes including low birth weight, infant mortality, and other physical health effects.[48] Mental health has been the most well studied health outcome associated with exposure to community violence.[49-57] Youth exposed to different forms of community violence, whether directly or indirectly, show elevated rates of symptoms related to acute or posttraumatic stress disorder, including disrupted sleep, anxiety, reduced awareness, and difficulty with concentration.[58-61] One study of low-income black urban children between the ages of 9 to 15 found that those who witnessed or were victims of violence showed symptoms of posttraumatic stress disorder (PTSD)

comparable to those of soldiers returning from war deployments, with symptoms increasing in a dose-dependent manner according to the number of violent acts witnessed or experienced. Symptoms included distractibility, intrusive and unwanted fears and thoughts, and feelings of not belonging.[62] The stresses that accompany inner-city living, including exposure to violence, are now being considered by some investigators as environmental exposures that contribute to asthma morbidity.[63]

Community Violence and Limits on Outdoor Activity

Community violence affects children in other ways as well. Children's outdoor activity in their neighborhood is influenced by both the child's and parent's perception of neighborhood safety.[64] Kalish et al. reported that parents were less likely to allow outside play as their degree of worry increased about a number of factors including crime, witnessing violence, being a victim of violence, drugs, gangs, and weapons.[65] A European study found that parents who perceived their neighborhoods as safe were three times as likely to encourage their children to go to local playgrounds as those who lived in neighborhoods that they perceived as unsafe.[66] Another concern is that children living in low-income, inner city environments are often unable to play in their own yards, local parks or community-based recreational programs because these areas don't exist or are not accessible to them. Even children with access to parks and a yard outside their home are unable to play because the community is not safe.[67] There is some evidence that gender differences may affect perceptions of neighborhood safety and playing outside. One study in Texas found that boys' perceptions of neighborhood safety were not significantly related to playing outside; however, girls' perceptions that their

neighborhood was safe were associated with more outdoor play.[68] A study of adult residents of 55 neighborhoods in Washington, DC found an association between levels of violent crime and fear. Overall, women were much more likely to be fearful and to refrain from walking outside; however, in high violence neighborhoods, men and women were equally fearful [69] The combination of violence outside the home and more prevalent allergen exposures inside the homes of many inner-city residents may lead to more time spent in indoor environments that contribute to asthma morbidity. These settings can lead to asthma exacerbations and may speed up disease development.[63]

Limits on Outdoor Play, Body Mass Index and Physical Activity

It is unclear whether community violence that causes children to be kept indoors is related to a decrease in physical activity or increased Body Mass Index (BMI). In one inner city area of New York City, children's physical activity levels were negatively associated with parental concern about safety in the neighborhood. Children in the inner city played outside of their homes less frequently, spent less time playing outside and engaged in less physical activity overall compared to children in a nearby suburban area. Nearly 60% of the parents in the inner city believed it was dangerous to let their children play outside compared to 8% in the suburban area.[70] In a study of adults residing in public housing projects in Chicago, perceptions of violence predicted subjects' fear of walking outside their homes, but fear of walking was not associated with reported physical activity.[71] Researchers from the CDC analyzed data from the 1996 Behavioral Risk Factor Surveillance System and found that respondents who perceived their neighborhood to be unsafe

were less likely to be physically active.[72] In a national sample of three year old children, mothers' perceptions of neighborhood safety were related to their children's TV viewing time but not to their outdoor play time or risk for obesity.[73] Mitchell et al. studied the association of hours of objectively measured sedentary behavior and odds of being obese, and found that sedentary behavior was positively associated with obesity in children.[74]

Asthma and BMI

Obesity is also of concern because of its association with asthma. In the National Survey of Child Health 2003-2004, older children ages 7-17 had a significant association between obesity and asthma.[75] There is also research showing that asthmatic children that are obese have greater asthma morbidity than other asthmatic children.[76] A study of over 2500 children in Indiana found that overweight boys and girls were 3.1 and 1.8 times more likely to have asthma than their normal weight peers, respectively.[77] Sensitization to allergens may also play an important role in this relationship. Visness et al. found that obesity was associated with asthma among children in National Health and Nutrition Examination Survey (NHANES) 1999-2006. The association was stronger in children who were not sensitized to common allergens compared to those who were sensitized to at least one allergen.[78] In NHANES 2005-2005 obese and overweight children had higher levels of total serum IgE than normal weight children. Obese children were more likely to be sensitized to common allergens than normal weight children, although this relationship was largely influenced by sensitization to foods.[79]

Asthma and Environmental Tobacco Smoke

Another important exposure in inner-city homes is environmental tobacco smoke (ETS). A high proportion of inner-city asthmatic children live in homes with ETS exposure. Smoking is more prevalent amongst minorities and the poor.[80,81] ETS is also more common in low-income, urban communities than in other demographic groups.[82] Fifty-nine percent of the children in the NCICAS and 48% of the children in the ICAS had ETS exposure in the home.[40,83] Over 55% of homes with asthmatic children in an inner-city Baltimore study have at least one active smoker in the home.[84,85] Two-thirds of the homes had at least one resident smoker in the Urban Environment and Childhood Asthma birth cohort study, which includes sites in Baltimore, Boston, New York and St. Louis.[86] Exposure to ETS is believed to both cause and exacerbate asthma in children. The US surgeon general concluded that ETS exposure was related to an increased risk of children ever having asthma and having more severe asthma.[87,88] In the National Survey of Child Health 2003-2004, both younger (ages 0-6) and older children (ages 13-17) had a greater than 20% increase in the odds of having asthma if there was a smoker in the home. [75] A number of studies show that ETS exposure is associated with poor asthma outcomes including increased asthma symptoms,[80,89-91] illness-related school absences,[92,93] health-care use,[93] as well as decreased lung function.[80,89,93,94]

Asthma and Air Pollution

A limited number of epidemiologic studies suggest that air pollution can increase the incidence of asthma;[95,96] however, this finding is not consistent across all studies.[97] Acute increases in air pollution have been associated with asthma

morbidity in children.[98-100] Investigators with a birth cohort in Boston found an association between traffic-related air pollution and asthma incidence, but only among urban children with elevated exposed to violence.[47] In urban areas of North Carolina, investigators found increases in ozone-related hospital admissions for asthma that were associated with certain types of weather air masses.[101] A concern with air pollution is that disadvantaged groups, such as the poor, are more highly exposed to some pollutants.[102] A study in Southern California found elevated exposure to ozone was associated with race, ethnicity, and income. They determined that ozone exposure differences by race and ethnicity have decreased over time but, low income areas may be experiencing higher ozone exposure than high income areas which could lead to a higher burden of respiratory disease and morbidity for lower income groups.[103]

The Inner-City Asthma Study

The Inner-City Asthma Study (ICAS) is a multi-center intervention study sponsored by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institute of Environmental Health Sciences (NIEHS) of the National Institutes of Health (NIH). ICAS was conducted from August 1998 to July 2001 by investigators from Albert Einstein College of Medicine, Bronx, NY; Northwestern University Medical School, Chicago, IL; University of Texas Southwestern Medical Center, Dallas, TX; Mt. Sinai School of Medicine, New York, NY; Univ. of Arizona College of Medicine, Tucson, AZ; Boston University School of Medicine, Boston, MA; University of Washington School of Medicine, Seattle, WA.[40] The list of ICAS Principal Investigators is included in Appendix A. The list of publications from ICAS

is included in Appendix B. Asthmatic children were recruited in these 7 sites and enrolled if they met the following inclusion criteria:

1. Aged 5 to 12 years of age

2. Had moderate to severe asthma as defined by the child experiencing one overnight hospitalization for asthma or two emergency department visits for asthma during the 6 months prior to screening

3. Had a positive skin test (wheal size at least 2 mm greater than glycerin control) to at least one of 11 common indoor allergens: Dust Mite (*Dermatophagoides farinae* and *D. pteronyssinus*), cockroach (German and American mix), rat, mouse, *Alternaria*, *Cladosporium*, *Aspergillus* mix (*A. flavus, fumigatus, glaucus, nidulans, niger*), *Penicillium*, cat, and dog

4. Lived in a census tract in which at least 20% of households had a household income below the federal poverty line

5. Slept in the target home ≥5 nights per week

The ICAS study was designed to test the hypothesis that reducing environmental exposures in the homes of asthmatic children that were both sensitized and exposed to allergens and irritants in their homes would lead to a reduction in the children's asthma symptoms. The 12 month environmental intervention in the homes of asthmatic children involved tailored education and remediation of environmental triggers including cockroaches, dust mites, ETS, mold, furry pets, and rodents. Subjects and families randomized to the environmental intervention received a home-based program designed to reduce the asthmatic

subjects' exposure to allergens and irritants, which was intended to both directly provide environmental mitigation services and to instruct the family about the importance and techniques of environmental mitigation so that they could sustain the mitigation on their own after completion of the intervention year.

A clinical evaluation was conducted at baseline, which included skin prick testing (SPT) and questionnaire administration. There were 1059 children screened with 937 enrolled in the study. After the baseline clinical evaluation, trained evaluators visited the child's home to conduct a visual assessment to determine general information about the home as well as evaluate environmental exposure to pets, cockroaches, mold, moisture, environmental tobacco smoke (ETS), etc. Dust was collected from the child's bedroom using a standardized protocol during this visit. The home evaluation team collected separate, vacuumed dust samples from the child's bedroom floor and bed. Dust samples were analyzed for allergens of the dust mites *D. pteronyssinus* (Der p1) and *D. farinae* (Der f1), cockroach allergen (Bla g1), cat allergen (Fel d1), and dog allergen (Can f1) by means of an enzyme-linked immunosorbent assay (ELISA).[104]

ICAS measured community violence by asking participants about various types of violence in their neighborhoods in the 6 months prior to the interview. Increased exposure to community violence was associated with an increase of approximately 4 days with asthma symptoms in the two week period prior to the baseline assessment (6 days vs. 10 days, p=0.009).[105] Wright et al hypothesized that the increase in asthma morbidity in these children was due to either a physiological stress response to violence or to increased exposure to indoor

allergens from being kept inside more. All of the children in the ICAS were sensitized to at least one allergen and half of them received a home-based intervention targeting allergens and irritants like ETS that they were exposed to in their homes. The intervention led to significantly decreased asthma morbidity compared to the control group in both the intervention year and the year following the active intervention; however, the investigators did not account for exposure to violence in their analysis.[104] The analysis of violence exposure and asthma morbidity found that increased exposure to violence led to increased morbidity, but did not take into account the child's sensitization and exposure status. The relationship between community violence and indoor allergen exposure has not been fully explored, and the hypothesis that exposure to violence leads to higher asthma morbidity due to increased exposure to allergens from being kept inside has not been tested. To examine this hypothesis, I propose the following specific aims:

Specific Aims

1. Determine if the relationship between perceived community violence and asthma morbidity is modified by exposure/sensitization status at baseline.

2. Determine if perceived community violence modifies the effect of an environmental intervention to reduce indoor allergen levels on asthma morbidity outcomes.

3. Determine if a change in perceived community violence is followed by a change in reported asthma morbidity at subsequent follow-up interviews.

4. Determine if the effect of community violence measured through crime reports is the same as the effects of community violence measured through respondent perceptions?

Chapter 2: Allergen Exposure Influences the Relationship between Community Violence and Asthma Morbidity: The Inner City Asthma Study

Background

Asthma is a chronic respiratory disease, which affects more than 10 million children and disproportionately affects minority and socioeconomically disadvantaged children.[3] While current asthma prevalence and lifetime diagnosis of asthma are similar for blacks and whites, blacks are five times as likely to visit the emergency room for asthma and more than three times as likely to be hospitalized or to die from asthma as whites.[8,10]

The reasons for childhood asthma disparities are complex and involve genetic, community and environmental factors. One of the most important environmental exposures associated with asthma and allergic disease is exposure to indoor allergens, such as those from dust mites, cats, dogs, cockroaches, rodents, and molds.[11-18] It is estimated that up to 80% of school-age children with asthma are allergic to at least one common indoor allergen.[29,34] Studies have also clearly shown that allergen exposure can lead to both acute and chronic symptoms in sensitized asthmatics.[12,18,19,34,35] Inner-city children with asthma are more likely to be sensitized to indoor allergens than outdoor allergens,[38,39] and sensitization to cockroach allergen has been widely shown to be associated with asthma.[12,26-31]

Increased asthma incidence and morbidity has also been linked to community violence in inner-city children[42-44,105] and adults.[45] Community violence is typically measured with questionnaire items addressing exposure to violence at the neighborhood level that may or may not be directed toward the respondent and is not inclusive of exposure to violence in the home. National estimates of childhood exposure to community violence range from 24.8% to 29.7%.[41] Wheezing in early life has been associated with exposure to violence,[42,44] and exposure to violence may also modify the relationship between traffic-related air pollution and asthma in urban children.[47] Parents are less likely to allow children to play outside as their anxiety increases about rundown parks, crime, violence, drugs, gangs, and weapons.[65] There is some evidence that parental report of keeping children indoors due to fear of violence in the neighborhood was associated with increased asthma incidence and morbidity.[44]

In the Inner-City Asthma Study (ICAS), reports of relatively high exposure to community violence was associated at baseline with a higher number of days with asthma symptoms ($p=0.009$).[105] Exposure to violence was also correlated with parents' fear for their children's safety in the neighborhood and not letting their children play outside. Wright et al. hypothesized that the increase in asthma morbidity in these children was due to either a physiological stress response to violence or to increased exposure to indoor allergens from being kept inside.

We further examined the relationship between community violence and asthma morbidity in the ICAS study population while considering each child's allergen exposures and sensitizations. We hypothesized that allergen

exposure/sensitization status mediates the relationship between exposure to violence and asthma morbidity due to increased exposure to allergens in the home. The relationships between asthma and exposures to violence and allergens have been considered separately in a number of studies, but this is the one of the first studies to examine the interrelationships between community violence, allergen exposure and asthma.

Methods

Study Population and Design

To evaluate our hypothesis, we used data from ICAS, a multi-center randomized, controlled trial conducted from August 1998 to July 2001. The study design and methods utilized in ICAS have been described in detail elsewhere, and are summarized here.[40] Asthmatic children 5-11 years of age who were allergic to at least one indoor allergen were recruited at 7 sites (Boston, Bronx, Chicago, Dallas, Manhattan, Seattle and Tucson). A clinical evaluation was conducted at baseline, which included allergen skin prick testing (SPT) and questionnaire administration. Of the 1059 children screened, 937 were enrolled in the study. After the baseline clinical evaluation, trained evaluators visited the child's home to conduct a visual assessment to determine general information about the home. At this visit they also evaluated environmental exposure to pets, cockroaches, mold, moisture, environmental tobacco smoke (ETS), etc. Vacuumed dust samples were collected from the child's bed and bedroom floor using a standardized protocol and assayed with ELISA to determine concentrations of indoor allergens. All analyses were conducted using the baseline data from the ICAS obtained under a user agreement

with the ICAS data coordinating center (Rho, Inc., Chapel Hill, NC) after approval from the ICAS steering committee. All data were obtained without identifying information and this work was exempted from IRB approval by both the University of North Carolina at Chapel Hill and National Institutes of Health Office of Human Subjects Research.

Asthma Outcome Measure

The primary variable used to characterize asthma morbidity for this study was asthma symptom days, an endpoint previously validated for use in ICAS. Asthma symptom days is defined as the largest value among the following three symptoms reported by the caretaker over the two week period prior to the baseline clinical exam: 1. days experienced wheezing, tightness in the chest, or cough; 2. days experienced disrupted sleep due to asthma; 3. days had to slow down or discontinue play or physical activities because of asthma. Asthma symptom days was treated as a continuous variable.

Allergic Sensitization and Allergen Exposure

Allergic sensitization was determined by the results of skin prick testing conducted at the baseline clinical examination. The following indoor allergens were tested: dust mite (Dermatophygoides farinae and Dermatophygoides pteronyssinus), cockroach (mix of German and American), rat, mouse, mold (Alternaria, Cladosporium, Aspergillus, Penicillium), cat, and dog.[19] A positive skin test result was determined as a wheal size at least 3 mm greater than saline control. Exposure to indoor allergens was derived from the allergen levels determined from vacuumed dust samples collected during the study. Details of sample collection and allergen

measurement are provided elsewhere.[19] Previous studies have considered children to be exposed at levels above the proposed thresholds for allergic sensitization or asthma exacerbation.[19,34] For this study, children are considered exposed at allergen levels above 2 U/g for cockroach (Bla g 1), 2 µg/g for dust mite (Der f 1 or Der p 1), 1µg/g for cat (Fel d 1), and 2 µg/g for dog (Can f 1).[19,28,106] Dichotomous exposure/sensitization variables were created for each allergen along with a composite variable for exposure and sensitization to any of the allergens. Subjects were placed in one of two categories based upon the combination of their exposure status for an allergen, and whether they had a positive skin test to that allergen. Children had to have both a positive skin test to an allergen and exposure to that allergen (as defined above under Exposure to Indoor Allergens) to be considered sensitized and exposed.

Perceived Community Violence

Perceived community violence was measured using the Violence Score derived as the sum of affirmative answers to the violence questionnaire administered at the Baseline Clinical Evaluation. Caretakers were asked about the violence in their neighborhood that they had experienced, witnessed or heard about. The question was, “Did any of the following occur in your neighborhood during the past 6 months: a fight with a weapon, a violent argument between neighbors, a gang fight, a sexual assault or rape, a robbery or mugging”?. More than 99% of caretakers completed the violence questionnaire at baseline; summing their affirmative answers for each response option created a 6-level categorical variable for violence score (values of 0-5).

The violence questionnaire used in ICAS is a modified version of the violence exposure survey developed by Richters and Saltzman, and has been used in other studies to measure perceived community violence.[107-109] At the time ICAS was conducted, this method of assessing exposure was one of the best available and similar questionnaires have been used frequently to assess children's exposure to community violence.

Crime Data

We were also interested in determining if the exposure measured by the violence score could also be assessed using data not based on respondents' perceptions. We replaced the violence score from the ICAS data with census tract level crime data from the National Neighborhood Crime Study (NNCS) obtained from the Inter-University Consortium for Political and Social Research through the National Archive of Criminal Justice Data.[110] In NNCS crime counts were obtained from police departments as the number of specific crimes per census tract or were geocoded and combined to census tract counts from individual crime records by address and crime type. The average geocoding hit rate was 97%. Data from NNCS were available for 5 of the 7 sites (Boston, Chicago, Dallas, Seattle and Tucson). Census tract numbers were used to link ICAS data with 3-year aggregate crime data for 1999-2001, the timeframe during which the ICAS was being conducted. We considered all types of violent crime reported in the dataset, including murder, rape and aggravated assault. Number of assaults and assault rates were the most highly associated with violence score. These data included the sum of the number of aggravated assaults and the three-year average census tract aggravated assault

rate per 1000. Both measures of crime data were treated as continuous variables with estimates generated at percentile levels similar to the levels of the violence score.

Other Covariates

Presence of pets, evidence of cockroaches, household smoking and the housing deterioration score were determined by questionnaire responses and field staff observations. The housing deterioration score was derived by summing the number of problems in the home, including: water damage, evidence of leaks, damaged or rotting windows, cracks or holes in floors, chipped or peeling paint on walls or windows. Questionnaire responses were also used to assess caretaker behaviors and perceptions related to skipping the child's asthma medication, being afraid to let the child play outside or being afraid the child would be hurt by violence in the neighborhood, negative life events, unwanted thoughts and stress.

Statistical Analysis

We used general linear models to assess the effect of violence score on asthma symptoms days. In addition to exposure/sensitization and community violence interaction, the model included the covariates from the final model used by Wright et al (i.e. site, household income and employment, caretaker education, race, ethnicity, smoking in the home, perceived stress, unwanted thoughts, negative life events, being afraid to let children play outside, skipping asthma medications and housing deterioration score).[105] We then conducted backwards elimination with the Bayesian information criterion (BIC)[111] and the Akaike information criterion (AIC)[112] to determine if there was a more parsimonious model that would effectively and

more efficiently describe the relationships between asthma morbidity, community violence and allergen exposure and sensitization. The final model included site, household income and employment, caretaker education, race, smoking in the home, perceived stress, unwanted thoughts, being afraid to let children play outside and skipping asthma medications. The *a priori* p-value for significance testing of statistical interactions was set at 0.20. All analysis utilized PROC GLIMMIX in SAS software (SAS 9.2 x64, SAS Institute, Inc., Cary, NC).

Results

For the 937 children enrolled in ICAS, the average age was 7.7 years. The majority of the participants were male, had a household income less than $15,000, were allergic to cockroaches and dust mites and had evidence of cockroaches in their homes. Children who were both exposed and sensitized to cockroach allergen were more likely to be black, have household income less than $15,000, have evidence of cockroaches in their homes and also be both sensitized and exposed to mouse allergen, as shown in Table 1. Those who were not both sensitized and exposed to cockroach were more likely to have a caretaker that completed high school and have at least one employed household member.

Higher exposure to community violence, measured by violence score, was associated with higher asthma morbidity (Figure 2) independent of study site, household income and employment, caretaker education, race, ethnicity, smoking in the home, perceived stress, unwanted thoughts, negative life events, being afraid to let children play outside, skipping asthma medications and housing deterioration score, as previously described by Wright, et al.[105] Violence and cockroach

exposure/sensitization were found to interact: children exposed to high levels of community violence had more asthma symptom days, but only if they were also both exposed and sensitized to cockroach allergen (sensitized/exposed p_{trend} = 0.01, $p_{interaction}$ = 0.15). Figure 3 shows results from the final model after backwards selection. The interaction was independent of study site, SES, race, smoking in the home, skipping asthma medications, the caretaker's reported stress and fear to let children play outside (exposed/sensitized p_{trend} = 0.001, $p_{interaction}$ = 0.07). Although included in our original analysis, we found that Hispanic ethnicity and measures of negative life events and home deterioration did not help explain the relationships between community violence, cockroach allergen exposure/sensitization and asthma. After backwards elimination these variables were not included in the final analysis. Only four children with a violence score greater than 3 were exposed and sensitized to dust mite allergen. None of the children with a violence score greater than 3, and only three with a violence score greater than 1, were exposed and sensitized to dog or cat allergen (data not shown). Due to these low numbers, we were unable to further evaluate the relationships between violence and sensitization/exposure to dust mite, cat, dog and mouse allergens.

Among children who were exposed and sensitized to cockroach allergen, a higher number of assaults in their census tract was correlated with a higher number of asthma symptom days (p_{trend}=0.22, $p_{interaction}$ = 0.14; Figure 4). The relationship was similar to, but less marked than that seen with the violence score (Figure 3). There were no differences in asthma morbidity by census tract assault rate among the children sensitized and exposed to cockroach allergen (p_{trend}=0.89;Figure 5);

however, there was a distinct trend toward less asthma morbidity with a higher assault rate among those not sensitized and exposed to cockroach allergen (p_{trend}=0.09, $p_{interaction}$ = 0.22).

Discussion

Children exposed to high levels of community violence, as measured by either violence score or number of assaults in the census tract, have more asthma symptom days, but only if they are also exposed and sensitized to cockroach allergen. This finding provides some supportfor the hypothesis that violence in the neighborhood leads to children spending more time in their indoor environment which in turn increases their asthma symptoms if they are sensitized to the allergens in that environment. ICAS did not collect any information about the amount of time the child spent indoors so there is no way to directly assess this hypothesis, but studies have shown that community violence may lead parents to keep their children inside the home more and not allow them to play outside.[64-67] A study conducted in Hartford, Connecticut found that parents of 5-7 year old children were less likely to allow outside play as their degree of worry increased about crime and other safety risks.[65] A European study found that parents who perceived their neighborhoods as safe were three times as likely to encourage their children to go to local playgrounds as those who lived in neighborhoods that they perceived as unsafe.[66] Another concern is that children living in low-income, inner city environments are often unable to play in their own yards, local parks or community-based recreational programs because these areas do not exist or are not accessible to them. Even

children with access to parks and a yard outside their home are unable to play because the community is not safe.[67]

We found similar results for number of assaults in a census tract as for violence score, but not census tract assault rates; children who were sensitized and exposed to cockroach allergen had higher asthma morbidity if they lived in a census tract with a higher number of assaults, but not a higher assault rate. Assault rate normalizes the number of assaults across the population of the census tract which may dilute the effect of crime and violence in the neighborhood. For example, a more densely populated tract (6500 residents) with more than 300 reported assaults would have an assault rate similar to a less densely populated tract (4000 residents) with only 200 assaults. Community violence is not typically used as a measure of whether or not someone actually experiences violence or is a victim of a crime. It is more frequently used to measure awareness of violence and crime in a neighborhood or community, which could arise from witnessing, hearing about or being a victim of violence.[113] We would argue that a dense population could lead to more communication about violent crimes because people are living in closer proximity to one another and have more opportunities to discuss crimes and violence in the neighborhood that they have experienced, witnessed or heard about. As a result, we propose that the number of assaults is a better measure for community violence than assault rates.

The psychological stress experienced by people who are exposed to high levels of violence in their communities may affect asthma morbidity through various physiological mechanisms that are not yet completely understood, and which may

even begin in utero.[114] While we were able to control for some questionnaire-based stress variables, they do not fully reflect the individual physiological response linked to stress due to violence. It is also important to note that the stress variables used in the analysis came from the caretakers' responses to the questionnaires, not from the children. Parent and caretaker reports may provide a more accurate representation of the violence and crime that actually occur in a neighborhood, particularly for younger children, but they may not as accurately represent the child's exposure to violence and crime that occurs outside their immediate neighborhood, such as when they are at school.[108] We also did not have measurements of biomarkers linked to stress (e.g., C-reactive protein or cortisol). This analysis was cross-sectional, and we cannot address temporal effects of community violence on asthma morbidity. Exposure to crime and violence could be a marker for other factors that were not measured such as neighborhood deprivation, social cohesion and social capital.[115,116] However, measures of SES, home deterioration, perceived stress and negative thoughts were evaluated and did not explain the increase in asthma symptom days amongst those children exposed to high levels of violence and exposed/sensitized to cockroach allergen.

The number of children exposed to the highest levels of violence is small with 33 children having a violence score of 4 and only 15 children having a violence score of 5. Even with the small numbers, the relationship between community violence and cockroach allergen exposure and sensitization is compelling. The children who have the highest violence exposure and cockroach allergen exposure and sensitization experience many days with asthma symptoms, averaging more

than 12 days with symptoms out of the two week period prior to the baseline interview. This is equivalent to more than 300 days if we extrapolate that figure out over a year. If children living in high violence communities spend more time inside their homes, then the children exposed to the highest levels of community violence spend the most time exposed to the allergens in their homes. If they are sensitized to those allergens, then it follows that they have more asthma symptoms. This study looks at a national sample of asthmatic children, which is representative of inner-city asthmatic children around the country. We have direct measurements of allergic sensitization and allergen exposure for each child, along with extensive questionnaire data on a number of potentially important covariates. At the time ICAS was conducted, the questionnaire used to derive the violence score was one of the best available and similar questionnaires have been used frequently to assess children's exposure to community violence.[107-109] The crime data were obtained from police departments in five of the seven sites with an average geocoding hit rate of 97%. The five sites with crime data fall across the range of average violence scores so that sites with the lowest and highest violence exposure are represented.

The violence and crime in the community of an asthmatic child does impact asthma morbidity; in particular, exposure and sensitization to cockroach allergen seems to play an important role in this relationship. These findings support the hypothesis that higher asthma morbidity seen in children living in violent neighborhoods is at least partially due to them spending more time indoors leading to higher exposure to indoor allergens, specifically cockroach allergen. Public health programs and intervention studies targeting asthmatic children in inner-city areas

should consider the importance of the multiple exposures these children experience and how best to implement programs and interventions that can reduce asthma morbidity.

Table 1. Characteristics of the ICAS population overall and by cockroach sensitization and exposure status

Characteristic	Overall (N=937)	Exposed & Sensitized (N =262)	Not Exposed & Sensitized (N =638)
Demographics			
Age of child (yr)	7.7±0.1	7.8±0.1	7.6±0.1
Male sex (%)	62.7	60.7	63.5
Black (%)	39.9	52.3	35.1*
Hispanic (%)	42.7	40.5	42.6
Caretaker completed high school (%)	69.4	64.4	72.0*****
Household income <$15,000 (%)	60.3	68.9	55.9*****
At least one employed household member (%)	75.9	66.5	79.7*****
Asthma-related symptoms within 2 weeks before baseline (no. of days)			
Number of days with asthma symptoms	6.0±0.2	6.4±0.3	5.9±0.2
Positive skin tests (%)			
Cockroach allergen	59.9	100.0	43.3*****
Dust-mite allergen (Der p1 or Der f1)	53.2	55.9	52.2
Cat allergen	36.6	37.0	36.5
Mouse allergen	21.8	27.1	19.4*****
Dog allergen	14.5	13.7	14.1
Allergen exposures (%)			
Cockroach allergen (≥ 2 U/g)	39.0	100.0	14.0*****
Dust-mite allergen (Der p1 or Der f1, ≥ 2 µg/g)	34.3	32.1	35.0
Cat allergen (≥ 1 µg/g)	25.3	22.0	26.8
Mouse allergen (≥ 1 µg/g)	24.2	33.6	20.2*****
Dog allergen (≥ 2 µg/g)	32.0	29.7	32.7
Environmental exposures (%)			
Evidence of cockroaches	70.9	91.2	62.3*****
≥1 Current smokers in home	48.4	51.2	47.8
Water, dampness, or leaks in home in past 12 months	45.5	45.8	45.6
Dog currently living in home	16.6	15.8	17.0
Cat currently living in home	13.1	12.6	13.7
Sensitized & Exposed to Allergen (%)			
Cockroach	29.1	100.0	0.0*****
Dust-mite (Der p1 or Der f1)	23.1	22.1	23.4
Cat	9.5	9.4	9.6
Mouse	8.1	11.1	6.7*****
Dog	4.0	4.3	3.9

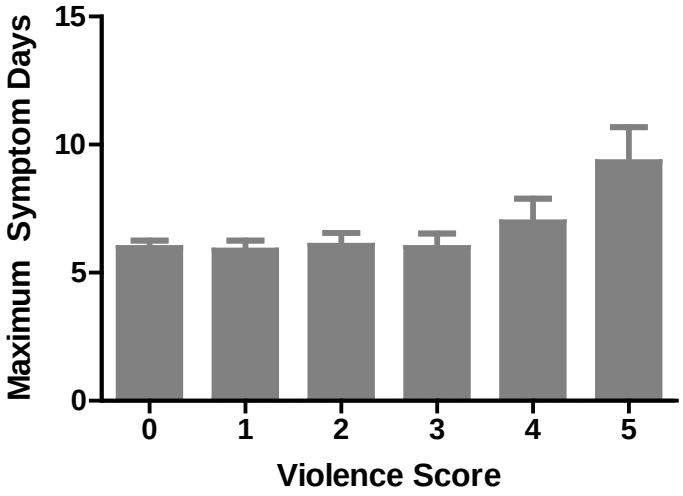
Table 1. (Continued)

Characteristic	Overall (N=937)	Exposed & Sensitized (N =262)	Not Exposed & Sensitized (N =638)
Violence Exposure			
Violence Score, n (%)***^**			
0	449 (48.1)	108 (41.2)	324(51.0)
1	213 (22.8)	48 (18.3)	155 (24.4)
2	126 (13.5)	47(17.9)	73(11.5)
3	98 (10.5)	38 (14.5)	58 (9.1)
4	33 (3.5)	14 (5.3)	19 (3.0)
5	15 (1.6)	7 (2.7)	6 (0.9)
Ever a victim of violence in neighborhood (%)	14.1	13.7	14.2
Sum of assaults in census tract (1999-2001)	150.7±4.3	169.9±9.7	144.6±4.9*
3-year average tract assault rate per 1000	13.4±0.44	18.1±13.3	11.9±0.4*
Site, n (%)***^**			
Boston	119 (12.7)	26 (9.9)	90 (14.1)
Bronx	134 (14.3)	60 (22.9)	68 (10.7)
Chicago	141 (15.1)	51 (19.5)	86 (13.5)
Dallas	135 (14.4)	48 (18.3)	82 (12.9)
New York	141 (15.1)	62 (23.7)	65 (10.2)
Seattle	127 (13.6)	2 (0.8)	122 (19.1)
Tucson	140 (14.9)	13 (5.0)	125 (19.6)
Caretaker Behaviors & Perceptions			
Ever Skipped Child's Asthma Medication (%)	35.4	35.8	35.8
Afraid to let child play outside (%)	33.9	40.8	30.6*****
Afraid child will be hurt by violence (%)	37.4	49.2	32.8*****
Negative Life Events Score (mean±SE)	2.5±0.1	2.2±0.1	2.7±0.1*****
Unwanted Thoughts (mean±SE)	1.8±0.1	1.7±0.1	1.9±0.1
Stress Score (mean±SE)	5.6±0.1	5.9±0.2	5.5±0.1

***** Chi-Square p-value <0.05

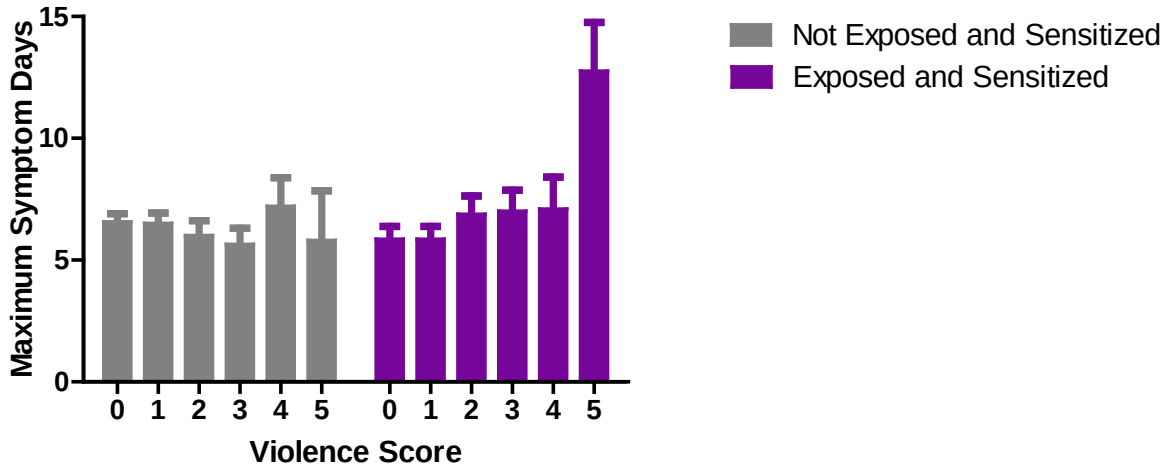
^ Mantel-Haenszel Chi-Square p-value <0.05

Figure 2. Asthma symptom days at baseline (mean, SE), by level of perceived exposure to community violence.*



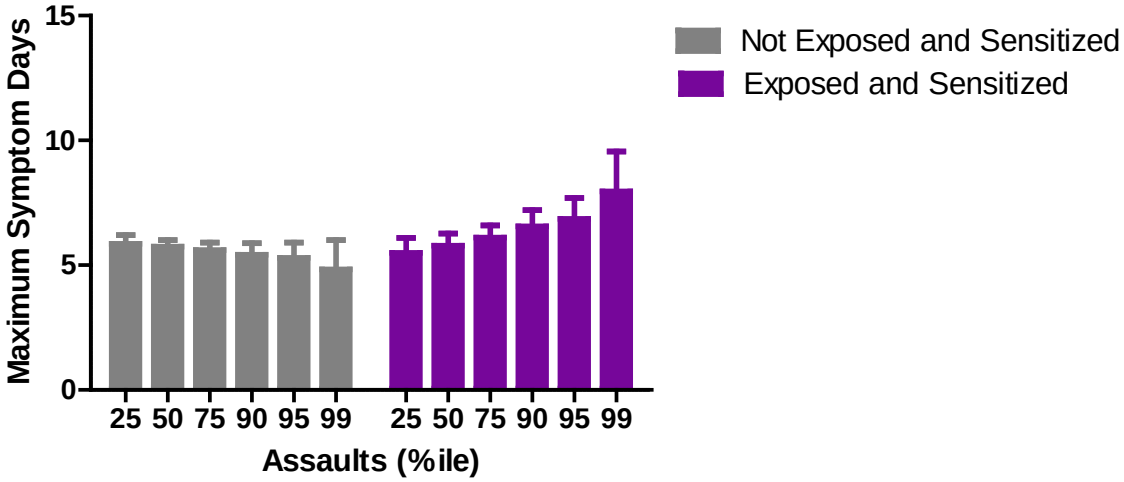
*Adjusted for site, household income and employment, caretaker education, race, ethnicity, smoking in the home, perceived stress, unwanted thoughts, negative life events, being afraid to let children play outside, skipping asthma medications and housing deterioration score.[105] Higher violence exposure was associated with higher asthma morbidity ($p_{trend} = 0.009$).

Figure 3. Asthma symptom days at baseline (mean, SE), by level of perceived exposure to community violence and cockroach allergen exposure/sensitization status*



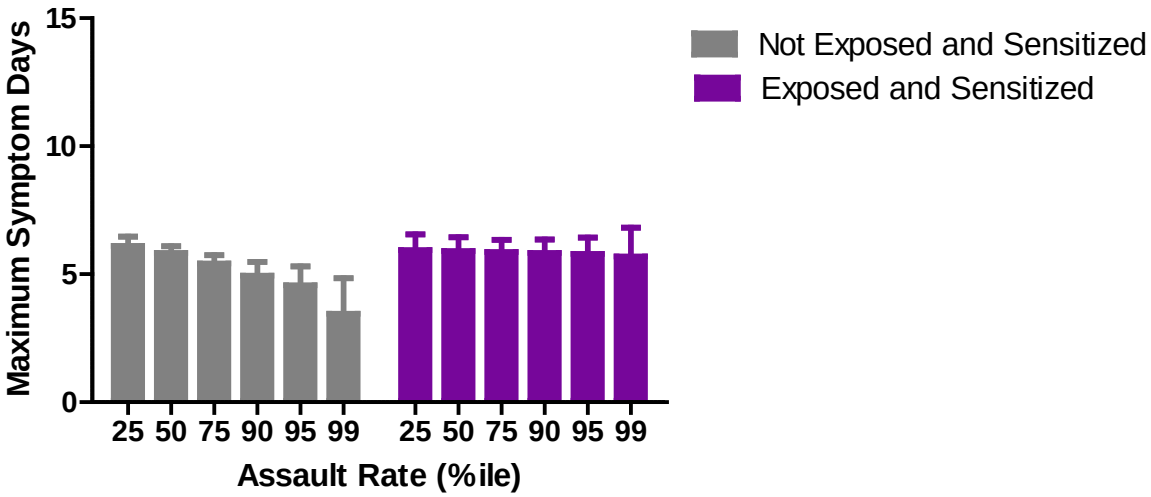
*Adjusted for site, household income and employment, caretaker education, race, smoking in the home, perceived stress, negative thoughts, afraid to let children play outside and skipping asthma medications. Higher violence exposure was associated with higher asthma morbidity, but only among those both sensitized and exposed to cockroach allergen (exp/sens $p_{trend} = 0.001$, $p_{interaction} = 0.07$).

Figure 4. Asthma symptom days at baseline (mean, SE), by level of census tract assaults and cockroach allergen exposure/sensitization status*



*Adjusted for site, household income and employment, caretaker education, race, smoking in the home, perceived stress, negative thoughts, afraid to let children play outside and skipping asthma medications. Living in census tracts with a higher number of assaults was associated with higher asthma morbidity, but only among those both sensitized and exposed to cockroach allergen (exp/sens p_{trend} =0.22, $p_{interaction}$ = 0.14).

Figure 5. Asthma symptom days at baseline (mean, SE), by level of census tract assault rate and cockroach allergen exposure/sensitization status*



*Adjusted for site, household income and employment, caretaker education, race, smoking in the home, perceived stress, negative thoughts, afraid to let children play outside and skipping asthma medications. Living in census tracts with a higher assault rate was not associated with higher asthma morbidity. Among those not both sensitized and exposed to cockroach allergen there was a trend for an inverse relationship between asthma morbidity and assault rate (not exp/sens p_{trend} =0.09, $p_{interaction}$ = 0.22).

Chapter 3: Effects of Community Violence on an Intervention to Reduce Asthma Morbidity in Children: The Inner City Asthma Study

Background

Children living in inner-city environments are often exposed to indoor allergens, pollution, violence, poverty and other stressors. Asthmatic children facing these exposures also have greater asthma morbidity and severity.[117] In recent years, a number of interventions have been conducted among children with asthma. These interventions are diverse and include in-home education,[104,118-125] home environment remediation,[104,118-124] school- or daycare-based programs,[126-130] and physician feedback and education,[131-133] among other strategies. Interventions targeting community violence or stress have been less frequently studied.[134] One of the largest and most comprehensive environmental interventions was the Inner City Asthma Study (ICAS) conducted in 1998-2001 at seven sites across the country.[40]

Previous reports from ICAS demonstrated the impact of both an asthmatic child's home and neighborhood environments on their asthma morbidity. Morgan et al. reported a reduction in asthma morbidity in ICAS after an intervention targeted to each participant's sensitizations and in-home exposures.[104] Wright et al found that increased community violence was associated with increased asthma morbidity at baseline, primarily in children that were exposed to high levels of community violence.[105]

At the time of that analysis, the allergen exposure data were not available, and it was hypothesized that the relationship between violence and asthma was likely occurring by one of two pathways: physiological stress or increased exposure to indoor allergens due to safety concerns about being outside. The decrease in morbidity in the ICAS study participants was most strongly correlated to reductions in cockroach and dust mite allergens; however, the analysis was not stratified by or adjusted for exposure to violence. Blood samples were not collected from the ICAS participants so there is no way to go back and assess the potential of the physiological stress pathway as the pathway by which community violence leads to greater asthma morbidity by looking at biomarkers related to stress that could have resulted from violence exposure. However, there is good data on allergic sensitization at baseline and allergen exposure throughout the course of the two years of follow-up. With this data, the allergen pathway can be assessed to determine if it is possible that exposure to community violence leads to increased asthma morbidity because of increased exposure to allergens due to more time indoors. The ICAS intervention was effective in reducing both cockroach allergen and asthma morbidity.[104] If community violence affects asthma through the allergen pathway, we would expect to see differing effects of the intervention at the various levels of violence exposure. The objective of this study was to determine if community violence influences the effect of the ICAS environmental intervention to reduce indoor allergen levels on asthma morbidity outcomes.

Methods

Study Population and Design

We used data from the ICAS which is a multi-center randomized, controlled trial conducted from August 1998 to July 2001. The study design and methods used in ICAS have been described in detail elsewhere, and are summarized here.[40] Asthmatic children 5-11 years of age who were allergic to at least one indoor allergen were recruited at seven sites (Boston, Bronx, Chicago, Dallas, Manhattan, Seattle and Tucson). Clinical evaluations, which included questionnaire administration, were conducted at baseline and after one year. Skin prick testing (SPT) was conducted at the baseline clinical evaluation. Of the 1059 children screened, 937 were enrolled in the study. Vacuumed dust samples were collected from the child's bed and bedroom floor using a standardized protocol and assayed with ELISA to determine concentrations of indoor allergens.

The ICAS included a 12-month environmental intervention designed to reduce exposure to allergens and irritants in the homes of enrolled children. The intervention was customized based on each child's skin-test–sensitization profile and environmental exposures reported by the caretaker or observed by the study staff at the baseline home evaluation. Each home in the intervention group received up to six intervention modules that targeted remediation of exposure to dust mites, smoking in the home, cockroaches, pets, rodents, and mold. There was an educational component to each module that was delivered by a trained environmental counselor. Professional pest control services were provided for homes that had cockroach or rodent infestations. All of the homes received

impermeable mattress covers for the child's bed and a HEPA-filtered vacuum cleaner. A HEPA air purifier was provided for the child's bedroom in homes where children were exposed to tobacco smoke, pet allergens or mold.

All analyses were conducted using data from the ICAS obtained under a user agreement with the ICAS data coordinating center (Rho, Inc., Chapel Hill, NC) after approval from the ICAS steering committee. All data were obtained without identifying information and this work was exempted from IRB approval by both the University of North Carolina at Chapel Hill and National Institutes of Health Office of Human Subjects Research.

Outcome Measures

The variable used to characterize asthma morbidity for this study was asthma symptom days, an endpoint previously validated for use in ICAS. Asthma symptom days was defined as the largest value among the following three symptoms over the two week period prior to each CATI-assisted follow-up phone interview conducted every two months: 1. days experienced wheezing, tightness in the chest, or cough; 2. days experienced disrupted sleep due to asthma; 3. days had to slow down or discontinue play or physical activities because of asthma.

Allergic Sensitization

Allergic sensitization was determined from the results of skin prick testing conducted at the baseline clinical examination for the following indoor allergens: dust mite (*Dermatophygoides farinae* and *Dermatophygoides pteronyssinus*), cockroach (mix of German and American in one test), rat, mouse, mold (*Alternaria, Cladosporium, Aspergillus, Penicillium*), cat, and dog.[19] A positive skin test result

was determined as a wheal size at least 3 mm greater than that resulting from the test with a saline control.

Exposure to Cockroach Allergen

Exposure to cockroach allergen was derived from the allergen levels determined from vacuumed dust samples collected from the child's bed and bedroom floor at six month intervals beginning at baseline. Details of sample collection were provided elsewhere.[19] Allergen concentrations were determined by ELISA assays, log-transformed and treated as continuous variables for analysis. For this study, children were considered exposed at allergen levels above 2 U/g of cockroach allergen (Bla g 1), the proposed sensitization threshold.[19,28]

Community Violence

Community violence was measured using the Violence Score derived as the sum of affirmative answers to the violence questionnaire administered at the baseline and follow-up clinical evaluations. Caretakers were asked about the violence in their neighborhood that they had experienced, witnessed or heard about. The question was, "Did any of the following occur in your neighborhood during the past 6 months: a fight with a weapon, a violent argument between neighbors, a gang fight, a sexual assault or rape, a robbery or mugging"?. More than 99% of caretakers completed the violence questionnaire at baseline, and more than 83% completed it at the follow-up clinical visit at the end of one year. To evaluate the effect of a change in violence on asthma morbidity, we took the difference of the violence score at baseline and the follow-up evaluation to create a variable for change in violence.

Statistical Analysis

The outcome variable of asthma symptom days, the log-transformed cockroach allergen concentrations measured in both the bedroom floor and bed, and the violence score were all treated as continuous variables. All analyses were done with linear mixed models with fixed effects for visit and adjustment for baseline symptoms and study site. The *a priori* p-value for significance testing of statistical interactions was set at 0.20. Participants were required to have had at least one follow-up assessment for asthma morbidity and one follow-up assessment of allergens levels to be included in the analysis, leaving 869 of the original 937 participants in this analysis.

Previous analysis showed that asthma morbidity and cockroach allergen exposure decreased in both the control and intervention groups, with a greater decrease in the intervention group.[104] Because of the decreases in both groups, we evaluated all participants for relationships between cockroach allergen exposure, allergic sensitization, community violence and asthma morbidity, irrespective of treatment group assignment. Addressing our primary objective required that we include a three-way interaction term (violence*cockroach allergen*cockroach sensitization) in the model. As a result, we had limited power to assess additional variables for confounding. All analyses were conducted with SAS software (SAS 9.2 x64, SAS Institute, Inc., Cary, NC).

Results

For the 937 children enrolled in ICAS, the average age was 7.7 years. The majority of the participants lived in a household with an income less than $15,000,

were allergic to cockroaches and dust mites and had evidence of cockroaches in their homes. More than 60% of the children were male. Participants allergic to cockroaches were more likely to be black, have household income less than $15,000, have evidence of cockroaches and be exposed to cockroach allergen in their homes, be sensitized to other indoor allergens and be exposed to mouse allergen (Table 2). Those who were not sensitized to cockroach allergens were more likely to have at least one employed household member and have a cat living in the home.

Overall, there was a decrease in asthma symptom days per two week reporting period with a one log unit decrease in cockroach allergen exposure in the bed or bedroom floor (Figures 6 and 7, respectively). Among those sensitized to cockroach allergen, the children with the highest violence scores had the greatest reduction in asthma morbidity following a decrease in cockroach allergen exposure in the bed or bedroom floor. The children not sensitized to cockroach allergen also had a decrease in their asthma symptom days with a decrease in cockroach allergen exposure, but the decrease in symptom days did not vary by level of violence exposure. Children not sensitized to cockroach had a decrease in symptom days following a decrease in cockroach allergen across the levels of violence score that ranged from 0.14 to 0.25 days and 0.24 to 0.28 days for the bedroom bed and bedroom floor, respectively. The children that were sensitized to cockroach allergen saw decreases of 0.17 to 0.58 days after a decrease in cockroach allergen in the bed and decreases of 0.13 to 0.43 days after a decrease in cockroach allergen in the bedroom floor across levels of the violence score.

The greatest decrease in morbidity after a one log unit decrease in cockroach allergen in the child's bed or bedroom floor was found in the children who had the highest community violence exposure and were also sensitized to cockroach allergen. The children exposed to the highest level of violence and sensitized to cockroach allergen had an average difference of -0.58 symptom days after a decrease in cockroach allergen in their beds compared to a difference of -0.14 symptom days for those children not sensitized to cockroach. This three-way interaction between cockroach sensitization, community violence and change in cockroach allergen was seen when considering both allergen exposure from the bedroom bed (Figure 6, $p_{interaction}$ = 0.20) and bedroom floor (Figure 7, $p_{interaction}$ = 0.24). When we attempted to control for potential confounders (e.g., Income, Race, Skipping Medications, Parents Afraid to Let Children Play Outside and Smoking), the results had similar magnitude and trends but were no longer significant ($p_{interaction}$ = 0.5). Figure 8 shows a representative example for the bedroom bed.

We also evaluated whether a change in community violence exposure would lead to a change in asthma morbidity (data not shown). There were no statistically significant differences between groups; however, the overall trends indicate that children with the greatest decrease in violence exposure (a decrease in violence score of 3 or more levels between the baseline and follow-up examination) had the greatest decrease in asthma symptom days from baseline to 24 months (approximately 5 days per 2 week reporting period), and those with the greatest increase in violence exposure (an increase in violence score of 2 or more levels) had

the smallest decrease in symptom days at 24 months (approximately 3 days per 2 week reporting period).

Discussion

A number of environmental intervention studies have been conducted with inner-city asthmatic children in an attempt to reduce asthma morbidity by reducing environmental exposures associated with asthma exacerbations. These interventions are diverse and include in-home education,[104,118-125] home environment remediation,[104,118-124] school- or daycare-based programs,[126-130] and physician feedback and education,[131-133] among other strategies. Intervention studies targeting community violence or stress have been less frequently conducted.[134] ICAS was one of the first multi-center environmental intervention trials in asthmatic children in the United States. The multi-component strategy that targeted each child's sensitization and exposure profiles was effective at reducing environmental exposures in the children's homes and decreasing their asthma morbidity.[104]

We evaluated the ICAS participants for interactions between cockroach allergen exposure, allergic sensitization, community violence and asthma morbidity, irrespective of treatment group assignment as both asthma morbidity and cockroach allergen exposure decreased in both the control and intervention groups.[104] Children sensitized to cockroach allergen and exposed to high levels of community violence had greater reductions in their asthma morbidity following a decrease in their cockroach allergen exposure than non-sensitized children. The children that were not allergic to cockroach also had decreases in asthma morbidity, which could be due to decreases in other allergens that they were sensitized to (e.g., dust mite) or

the Hawthorne effect, an improvement in the outcomes of participants of a randomized trial due to simply being in a study, which is frequently seen in intervention studies like ICAS.[135] If cockroach sensitized children living in high violence neighborhoods spend more time indoors, then improving their indoor environment should have a greater impact on their asthma because they spend more time exposed to the allergens in their homes. These findings support the hypothesis that higher asthma morbidity seen in children exposed to violence in their neighborhoods is due, at least in part, to spending more time indoors leading to higher exposure to indoor allergens, specifically cockroach allergen.

Decreases in allergen exposure were associated with decreases in asthma morbidity, and we sought to evaluate whether decreases in community violence exposure were also associated with decreased asthma morbidity. The Moving to Opportunity study in Boston demonstrated that asthmatic children who moved from apartments in high poverty census tracts to tracts with low poverty saw improvement in their asthma.[136] The investigators recognized the potential asthma triggers present in the high poverty areas, including allergens and stress, and hypothesized that the move would benefit the participants' health; however, they did not measure allergen levels to determine changes in exposure, nor did they monitor the amount of time the children spent outside. They did measure exposure to neighborhood violence and found a marked decrease in violence exposure for those who moved into the low poverty areas.

To evaluate the effect of a change in violence on asthma morbidity in the ICAS study population, we took the difference of the violence score at baseline and

the 12 month follow-up visit. The greatest decrease in violence exposure (≥ 3 unit decrease), was associated with the greatest decreases in asthma symptom days from baseline to 24 months (approximately 5 days per 2 week reporting period); although, there were no statistically significant differences. Additional studies would be needed to determine whether reductions in community violence could reduce asthma morbidity in inner-city children and what role cockroach allergen exposure and sensitization would have in that process.

There are some limitations to this study. The number of children exposed to the the highest levels of violence is small, with only 48 children having a violence score of 4 or 5. Even with small numbers, the results are convincing that asthmatic children sensitized to cockroach allergen respond differently to a decrease in cockroach allergen exposure across levels of violence score. Also, we have only one measurement of allergic sensitization, which occurs at baseline. It is possible that some of the children, that did not have a positive skin prick test at baseline, became sensitized at some point during the 2 year study. It is unlikely that enough children could have become sensitized to cockroach allergen after the baseline exam to change the results of this study. All of the children were allergic to at least one allergen at baseline and 60% were allergic to cockroach allergen. Younger children tend to be allergic to food allergens such as milk and egg and transition to sensitization to inhalant allergens like dust mite and cockroach around 3-5 years of age.[20,137,138] The children not sensitized to cockroach allergen were slightly younger with a mean age of 7.4 vs. 7.9 years in the sensitized children, but all of the children were at least 5 years of age at the time of enrollment.

We also did not have truly longitudinal data on community violence exposure. The violence questionnaire was administered only at the baseline and 12 month follow-up examinations, with no way to determine when changes in community violence exposure occurred or if any changes occurred during the second year of follow-up. This questionnaire also did not differentiate between learning about, witnessing or being a victim of violence so we had no way to determine if children who were victims of violence had different responses to the intervention than children who only heard about violence in their communities. One way violence exposure is thought to lead to greater asthma morbidity is through physiological mechanisms related to stress. Although questionnaires about stress and negative life events were administered, they did not ascertain information about stress related to community violence and no biomarker data (e.g., C-reactive protein or cortisol) were available for this study population.

In inner-city neighborhoods, asthmatic children face multiple exposures that may exacerbate their asthma. This study demonstrates that asthmatic children exposed to high levels of violence in their communities and sensitized to cockroach allergen received the most benefit from an environmental intervention targeting exposures in homes. It is plausible that reducing cockroach allergen levels would have the greatest benefit for children who are sensitized to cockroach allergen and spend the most time exposed to their home environment. If the children exposed to community violence spend more time inside their homes because of the danger outside the home, then it would follow that the children exposed to the highest levels of community violence spend the most time exposed to the allergens in their homes.

We do not discount the physiological effects that may also be occurring in these children as a result of community violence exposure, but we do caution physicians, researchers and public health practitioners not to ignore the importance of the indoor environment when developing treatment, study and public health policy plans for asthmatic children in urban, inner-city environments. Improving both the home and community environment will eventually help not only asthmatic children, but likely other community residents as well; however, improving the home environment by decreasing cockroach allergen exposure is likely a more feasible intervention than decreasing community violence. While the latter has been tried, it is a difficult, often lengthy task that is frequently unsuccessful.[139-141] In contrast, there are validated methods for reducing cockroach exposure that are safe, highly effective and relatively inexpensive.[118,142,143] To our knowledge there has not been an asthma intervention that targeted both the indoor environment and violence in the community. This analysis has demonstrated that there are important interactions between cockroach allergen exposure, sensitization to cockroach and community violence exposure that need to be considered when attempting to intervene to improve the health of inner-city children with asthma.

Table 2. Characteristics of the ICAS population overall and by cockroach sensitization status

Characteristic	Overall (N=937)	Sensitized (N =561)	Not Sensitized (N =375)
Demographics			
Age of child (yr±SE)	7.7±0.1	7.9±0.1	7.4±0.1*
Male sex (%)	62.7	63.1	62.1
Black (%)	39.9	45.3	32.0*
Hispanic (%)	42.7	43.7	41.3
Caretaker completed high school (%)	69.4	67.2	72.7
Household income <$15,000 (%)	60.3	64.7	53.8*****
At least one employed household member (%)	75.9	73.2	79.9*****
Asthma-related symptoms within 2 weeks before baseline (no. of days)			
Number of days with asthma symptoms	6.0±0.2	6.1±0.2	5.9±0.3
Positive skin tests (%)			
Cockroach allergen	59.9	100.0	0.0*****
Dust-mite allergen (Der p1 or Der f1)	53.2	57.5	46.7*
Cat allergen	36.6	39.6	32.3*
Mouse allergen	21.8	26.2	15.2*****
Dog allergen	14.5	16.0	12.3
Allergen exposures (%)			
Cockroach allergen (≥ 2 U/g)	39.0	48.7	24.6*****
Dust-mite allergen (Der p1 or Der f1, ≥ 2 µg/g)	34.3	33.3	36.0
Cat allergen (≥ 1 µg/g)	25.3	21.5	31.0*
Mouse allergen (≥ 1 µg/g)	24.2	27.9	18.9*****
Dog allergen (≥ 2 µg/g)	32.0	29.3	36.0*
Environmental exposures (%)			
Evidence of cockroaches	70.9	79.6	58.0*****
≥1 Current smokers in home	48.4	48.5	48.3
Water, dampness, or leaks in home in past 12 months	45.5	46.2	44.5
Dog currently living in home	16.6	16.0	17.6
Cat currently living in home	13.1	10.9	16.4*
Sensitized & Exposed to Allergen (%)			
Cockroach	29.1	48.7	0.0*****
Dust-mite (Der p1 or Der f1)	23.1	23.2	23.0
Cat	9.5	9.5	9.7
Mouse	8.1	9.6	5.9
Dog	4.0	4.1	3.9

Table 2. (Continued)

Characteristic	Overall (N=937)	Sensitized (N =561)	Not Sensitized (N =375)
Violence Exposure			
Violence Score, n (%)***^**			
0	449 (48.1)	258 (46.0)	190(51.1)
1	213 (22.8)	115 (20.5)	98 (26.3)
2	126 (13.5)	89 (15.9)	37(10.0)
3	98 (10.5)	66 (11.8)	32 (8.6)
4	33 (3.5)	23 (4.1)	10 (2.7)
5	15 (1.6)	10 (1.8)	5 (1.3)
Ever a victim of violence in neighborhood (%)	14.1	13.9	14.5
Sum of assaults in census tract (1999-2001)	150.7±4.3	158.4±5.8	140.6±6.5*
3-year average tract assault rate per 1000	13.4±0.44	14.8±0.7	11.5±0.5*
Site, n (%)***^**			
Boston	119 (12.7)	69 (12.3)	50 (13.3)
Bronx	134 (14.3)	105 (18.7)	29 (7.7)
Chicago	141 (15.1)	81 (14.4)	60 (16.0)
Dallas	135 (14.4)	102 (18.2)	33 (8.8)
New York	141 (15.1)	103 (18.4)	38 (10.1)
Seattle	127 (13.6)	35 (6.2)	91 (24.3)
Tucson	140 (14.9)	66 (11.8)	74 (19.7)
Caretaker Behaviors & Perceptions			
Ever Skipped Child's Asthma Medication (%)	35.4	36.5	33.9
Afraid to let child play outside (%)	33.9	34.9	32.5
Afraid child will be hurt by violence (%)	37.4	40.5	32.9*****
Negative Life Events Score (mean±SE)	2.5±0.1	2.4±0.1	2.7±0.1
Unwanted Thoughts (mean±SE)	1.8±0.1	1.8±0.1	1.9±0.1
Stress Score (mean±SE)	5.6±0.1	5.6±0.1	5.6±0.2

***** Chi-Square p-value <0.05

^ Mantel-Haenszel Chi-Square p-value <0.05

Figure 6. Change in asthma symptom days with a 1 log unit decrease in cockroach allergen exposure in the <u>child's bed</u>, stratified by cockroach sensitization

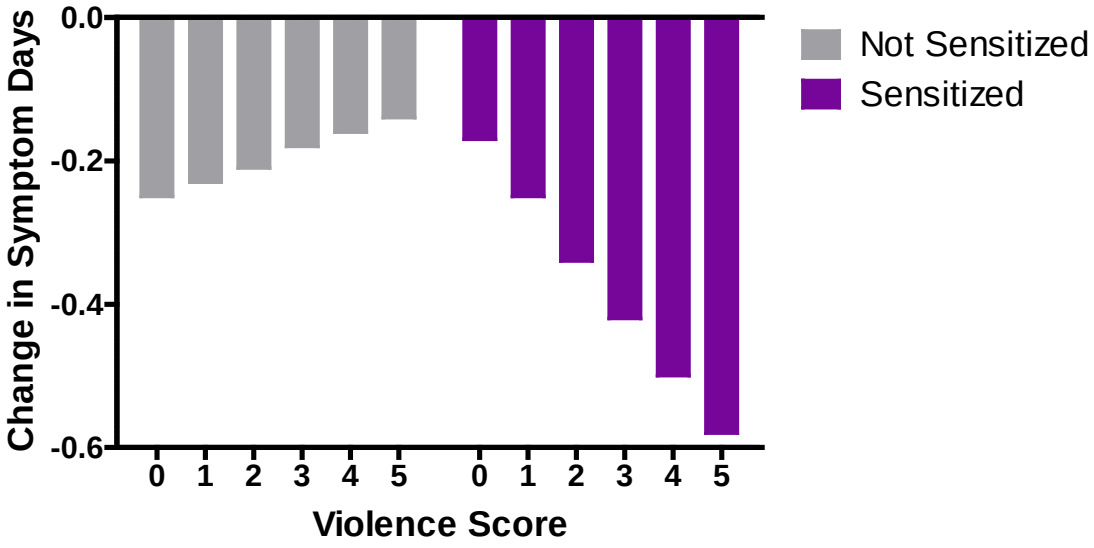


Figure 7. Change in asthma symptom days with a 1 log unit decrease in cockroach allergen exposure in the child's bedroom floor, stratified by cockroach sensitization.

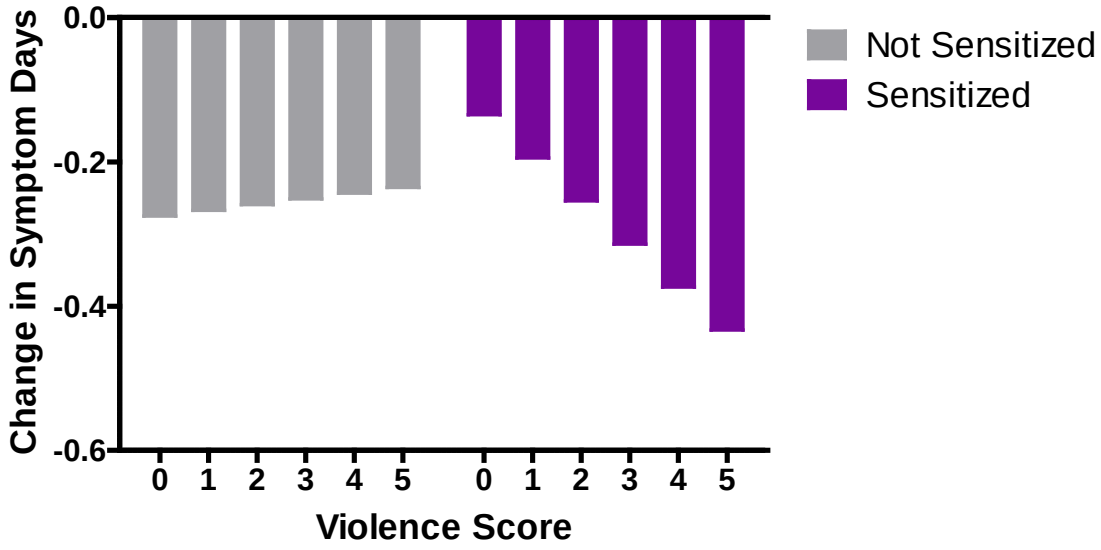
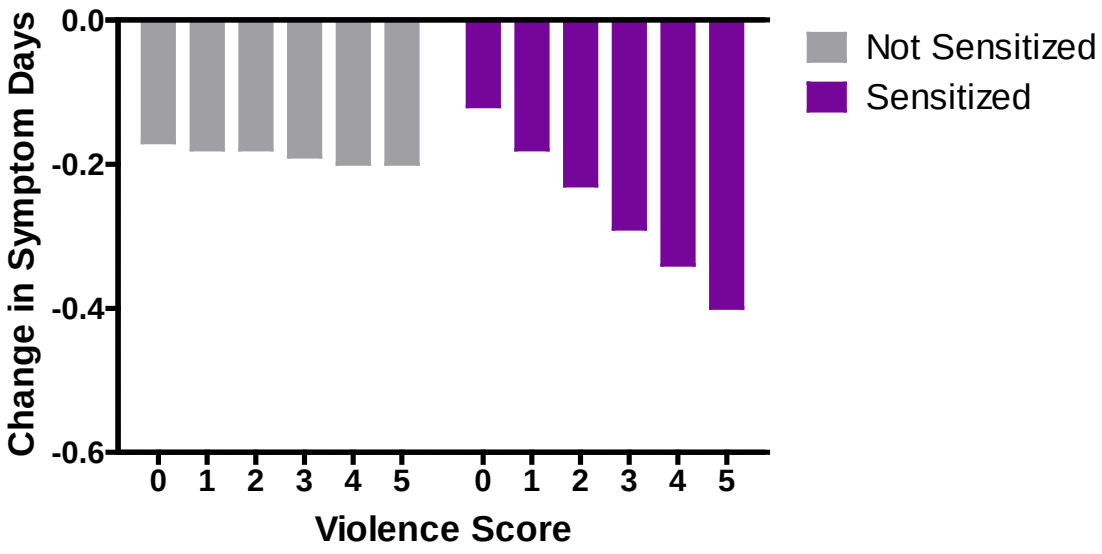


Figure 8. Change in asthma symptom days with a 1 log unit decrease in cockroach allergen exposure in the child's bed, stratified by cockroach sensitization.*



*Adjusted for income, race, skipped medications, parents afraid to let children play outside and smoking.

Chapter 4: Discussion

Summary of Findings

Asthmatic children exposed to high levels of community violence, as measured by a questionnaire-based violence score, have more asthma symptom days, but only if they are also exposed and sensitized to cockroach allergen. I found similar results for number of assaults in a census tract as for violence score, but not census tract assault rates. In this cross-sectional analysis of ICAS baseline data, children who were sensitized and exposed to cockroach allergen had higher asthma morbidity if they had a high violence score or lived in a census tract with a relatively high number of assaults, but not if they lived in a census tract with a relatively high assault rate.

Morgan et al showed that a decrease in allergen exposure was associated with decreases in asthma morbidity over the course of the two year ICAS study, but did not consider the possible effects of violence exposure in the analysis.[104] I incorporated violence score into the analysis along with cockroach sensitization status and found that children sensitized to cockroach allergen and exposed to high levels of community violence had greater reductions in their asthma morbidity following a decrease in their cockroach allergen exposure than non-sensitized children. Sensitized children saw greater improvement in their asthma morbidity following intervention as violence score level increased. Non sensitized children also

saw improvement in their asthma following a decrease in cockroach allergen exposure, but the decrease was similar across all levels of violence score and generally less than that of the sensitized children.

To evaluate if a change in violence exposure would also lead to a change in asthma morbidity, I considered the difference of the violence score determined at the baseline and 12-month follow-up visits and subsequent changes in asthma morbidity. There are some limitations to this analysis which are described below; however, the greatest decrease in violence exposure was associated with the greatest decrease in asthma symptom days; although, there were no statistically significant differences (Appendix C). More than 200 participants (28%) had a decrease in community violence exposure at the end of the first year of the study. Those whose violence score decreased by at least 3 levels (e.g., a violence score of 5 at baseline with a violence score of 0, 1 or 2 at the 12 month visit) had the greatest decrease in their asthma symptom days with a mean of 6.3 symptom days during the 2 weeks prior to the baseline visit and a mean of 2.7 symptom days during the 2 weeks prior to the 24-month visit.

If cockroach sensitized children living in high violence neighborhoods spend more time indoors where they are exposed to cockroach allergen, then improving their indoor environment should have a greater impact on their asthma because they spend more time exposed to the allergen. These findings support the hypothesis that higher asthma morbidity seen in children exposed to violence in their neighborhoods is due, at least in part, to spending more time indoors leading to higher exposure to indoor allergens, specifically cockroach allergen.

Study Limitations

This study has some limitations. Several factors that may affect the relationships between cockroach allergen exposure and sensitization, community violence and asthma morbidity were not measured in ICAS. For example, blood samples were not collected from ICAS participants, meaning biomarkers of stress and inflammation, such as cortisol or C-reactive protein could not be considered to estimate the actual physiologic effects that exposure to community violence may trigger. Although questionnaires were administered in an attempt to quantify the caretakers' levels of stress, they did not ascertain information about stress directly related to community violence exposure. It would have been helpful to have the questionnaires for violence and stress administered at more frequent intervals during the study and again at the final follow-up visit at the end of the second year; and have the time interval targeted in the violence questionnaire shortened from 6 months prior to the interview to 1-2 months prior to the interview. This information would have been useful in my attempts to determine if changes in violence were associated with changes in asthma morbidity. The data that are included in ICAS have information about the violence exposure in the six months prior to the baseline visit and the 12 month follow-up visit. If violence exposure changed between the visits, there is no way to determine if the change occurred at month 1 or month 8, for example. This could be particularly important if there is a lag between change in violence exposure and a related change in asthma morbidity.

ICAS also did not attempt to measure time spent indoors, outdoors or engaged in physical activity. Based upon findings from other studies, I am assuming

that asthmatic children living in areas with higher levels of violence spend less time playing outside and more time exposed to the environment in their homes but have no way to determine where the children enrolled in ICAS actually spent their time.[64-69] To participate in ICAS the children had to sleep in the caregiver's home at least 5 nights per week. Outside of the exposures in the caregiver's home, I do not have any information on additional exposures the participants had at school, childcare facilities, or homes of other family members or friends, etc. If the children exposed to higher levels of community violence did not actually spend more time indoors compared to children in less violent communities, then the differing response to community violence seen between the cockroach sensitized and non-sensitized participants (Figures 3, 6 and 7) would indicate that the physiological response to stress due to community violence is driving the increase in asthma morbidity seen at higher levels of violence exposure along with the possibility of a synergistic effect of community violence exposure and sensitization to cockroach allergen.

There is a slight possibility that children who were not sensitized to cockroach at baseline became sensitized over the course of the study. All of the children were allergic to at least one allergen at baseline and 60% were allergic to cockroach allergen. Younger children tend to be allergic to food allergens such as milk and egg and transition to sensitization to inhalant allergens like dust mite and cockroach around 3-5 years of age.[20,137,138] The children not sensitized were slightly younger with a mean age of 7.4 vs. 7.9 years in the sensitized children, but all of the children were at least 5 years of age at the time of enrollment. Overall, the non-sensitized children had a smaller decrease in asthma symptom days after a decrease in

cockroach allergen (Figure 6). If some of them became sensitized during the study, it could have attenuated the difference seen between the sensitized and not sensitized participants. If there were no differences between sensitization groups in asthma improvement after a decrease in cockroach allergen exposure, then the hypothesis that the association between community violence and asthma morbidity is partly driven by increased allergen exposure due to spending more time indoors would not be supported. This is not likely the case in this analysis as the greatest differences in the change in asthma symptom days occurs at the higher levels of violence exposure and there were only twelve children not sensitized to cockroach at baseline who had a violence score of at least 3, and only three who had a violence score of at least 4 who were also exposed to cockroach allergen at levels thought to be high enough to lead to sensitization.[28]

In the analysis comparing more objective measures of community violence with caretakers' perceptions, I was unable to access three year aggregate crime data for 2 of the 7 sites. Also, 2 of the 5 cities for which I had crime data did not report rape and sexual assault numbers at the census tract level out of concern for victims being able to be identified. Because of these unreported data, the composite violent crime statistic included in the dataset was not useful. I was also unable to create a crime score from the crime data to correlate directly with the violence score by using the same types of violence asked about in the questionnaire. This could have been used to directly compare caretaker perceptions with corresponding crime data and gain a better understanding of how accurately caretaker responses reflect the reported crime and violence in their community. Understanding this relationship

would provide an opportunity to use crime data as a surrogate for perceived violence and allow investigators to measure community violence in completed studies or those already underway that did not administer a violence questionnaire.

One concern with the assessment of confounders for Aim 1 was that some of the variables assessed for confounding might actually be on the mechanistic pathway (Figure 1); specifically perceived stress, negative life events, unwanted thoughts, being afraid to let children play outside and skipping asthma medications. In the questionnaire administered to generate the perceived stress variable (Appendix D), there are no questions related to stress arising from violence exposure. Also, the stress variable and violence score are not highly correlated, indicating that in this population, exposure to violence was not associated with an increase in stress as measured by the stress questionnaire. The negative life events questionnaire, which also assessed unwanted thoughts about these events (Appendix E), contains only 2 questions related to violence or crime out of 23. These questions ask the respondent about their home being broken into and if they or a member of the immediate family been assaulted or mugged in the previous year. As part of the violence questionnaire, caretakers were asked “Do you not let your children play outside because you are afraid they might be hurt by violence in this neighborhood?” The correlation between the responses to this question and the violence score is surprisingly low with 40% of the caretakers with the highest violence score of 5 responding that they were not afraid to let their child play outside and 23% of caretakers with a violence score of 0 responding they were afraid to let their children play outside. Being afraid to let children play outside can be

considered as a confounder because the low correlation indicates the variable, as derived, is not on the mechanistic pathway.

Still another concern is that increased violence may have caused difficulties for caretakers in getting asthma medication for the participants leading to skipped medications. This could occur because pharmacies may not be located in more violent areas or because of the potential danger in travelling to and from the pharmacy that keeps the caretaker from getting the medication. While this may have occurred for some of the caretakers who reported higher violence scores, the questions asked to determine if they ever skipped asthma medication did not deal with violence, fear of travelling to a pharmacy or lack of pharmacies close to the home with the exception of one question that asks if the caretaker had problems getting medication because the pharmacy did not have it or because it was hard to get to the pharmacy (Appendix F). Of the caretakers who said they did skip medications because the pharmacy did not have it or because it was hard to get to the pharmacy, none of them had a violence score of 5, only 6% had a violence score of 4 and 38% had a violence score of 0. In this study, it is valid to consider skipped medications as a confounder because the variable is derived in a way such that it is not on the mechanistic pathway.

Study Strengths

The ICAS was one of the first intervention studies of its kind, including a multi-component intervention targeted to each child's allergic sensitization and exposure profile along with incorporating questionnaires to assess psychosocial and community level factors that may play a role in asthma morbidity. At the end of the

study in 2001, ICAS was one of the largest asthma intervention studies ever completed with 937 children initially enrolled and more than 96% still enrolled after two years with 91.2% average contact. The ICAS was conducted at 7 sites around the country, which gave the study greater generalizability than many other asthma intervention studies. ICAS was also one of the few studies to measure allergic sensitization, allergen exposure and community violence in a cohort of asthmatic children. ICAS has direct measurements of allergic sensitization and allergen exposure for each child, along with extensive questionnaire data on a number of potentially important covariates. At the time ICAS was conducted, the questionnaire used to derive the violence score was one of the best available and similar questionnaires have been used frequently to assess children's exposure to community violence.[107-109] The crime data were obtained from police departments in five of the seven sites with an average geocoding hit rate of 97%. The five sites with crime data fall across the range of average violence scores so that sites with the lowest and highest violence exposure are represented.

Even though the number of participants exposed to the highest levels of violence as measured by the violence score was relatively small, they represent a very vulnerable group of asthmatic children. Approximately 5% of the children had a violence score of 4 or greater with almost 2% having a score of 5. However, of those with a violence score of 5, 75% were sensitized to cockroach and nearly half were both sensitized and exposed to cockroach allergen levels at or above 2 U/g, a level associated with a higher risk of incident asthma and cockroach sensitization.[28,35] Seventy percent of the children with a violence score of 4 were sensitized to

cockroach allergen, and 42% were both exposed and sensitized (Appendix G). While the percentage of children with the highest levels of community violence exposure is small, these children have the most asthma symptom days, are likely to be exposed to cockroach allergen and may need and benefit the most from interventions in both their communities and indoor environments. Even with the limitations noted above, this work still highlights the need to consider what asthmatic children are exposed to both inside and outside their homes, how these exposures interact and what effect these interactions may have on asthma interventions, particularly in inner-city populations.

Future Directions

There is an opportunity for more detailed assessments of community violence and crime exposure using more complex GIS designs that will account for the census tract or block where the residence is located, as well as the proximity to neighboring tracts or blocks that individuals are likely to be exposed to, and the violence and crime in those areas. Additional studies could also consider the individual components that make up the violence score to examine the possibility of a threshold effect or attempt to determine if one particular type of violence is driving the relationship with asthma morbidity. The components of the violence score could also be weighted to incorporate the potential for greater impact of one type of violence of another.

Air pollution is a potentially important exposure for inner-city asthmatic children and there may be a synergistic effect between air pollution and violence exposure, as shown in a birth cohort study in Boston.[47,98-100] ICAS did not

incorporate any measures of outdoor air pollution. A future study incorporating air pollution data into the ICAS dataset would provide an opportunity to consider the effects of air pollution on the relationships between community violence, allergen exposure and asthma. Additional studies are also needed to determine if reductions in community violence can be effective in reducing asthma morbidity in inner-city children. The limitations noted above make it difficult to determine if a decrease in violence score is associated with a subsequent decrease in asthma morbidity in the ICAS dataset.

Conclusions

It was hypothesized that the relationship between violence and asthma was likely occurring by one of two pathways: physiological stress or increased exposure to indoor allergens due to safety concerns about being outside.[105] Psychological stress can be seen as a social pollutant that can disrupt biological mechanisms that are also affected by environmental pollutants. When people experience stress, their body systems may not function as they would under normal homeostatic conditions. Regulation of the body's normal stress systems, such as the hypothalamic-pituitary-adrenal axis and the autonomic nervous system, may be altered, which could lead to changes in immune function. These changes can then lead to increased airway inflammation and airway reactivity, contributing to increases in asthma morbidity.[48,114,144] Blood samples were not collected from the ICAS participants so I cannot directly assess the potential of the physiological stress pathway as the pathway by which community violence leads to greater asthma morbidity by looking at biomarkers related to stress that could have resulted from violence exposure.

While these physiological effects may be occurring in these children as a result of community violence exposure, it is important to focus the limited resources available for asthma interventions on the programs that can have the most impact on asthma symptoms which are also cost effective. Improving the home environment by decreasing cockroach allergen exposure is likely a more feasible intervention than decreasing community violence. While the latter has been tried, it is a difficult, often lengthy task that is frequently unsuccessful.[139-141] There are validated methods for reducing cockroach exposure that are safe, highly effective and relatively inexpensive.[118,142,143] These methods have been refined in recent years, and are often even more effective at reducing cockroach infestations and allergens than the type of intervention used in ICAS.[143] At this time, there has not been an asthma intervention that targeted both the indoor environment and violence in the community.

This work highlights the importance of environmental exposures in both the homes and communities of inner-city asthmatic children. Asthmatic children exposed to high levels of violence in their communities and cockroach allergen in their homes have more symptoms, but also respond better to home-based environmental interventions to reduce their allergen exposure. Although the number of children who have both high violence exposure and cockroach allergen exposure is relatively small, they have an enormous number of days with asthma symptoms, equivalent to more than 300 days out of a year. If children living in high violence communities spend more time inside their homes, then the children exposed to the highest levels of community violence spend the most time exposed to the allergens in their homes.

I do not discount the physiological effects that may also be occurring in these children as a result of community violence exposure, but I do caution physicians, researchers and public health practitioners not to ignore the importance of the indoor environment when developing treatment, study and public health policy plans for asthmatic children in urban, inner-city environments.

Appendix A: ICAS Principal Investigators

Ellen F. Crain, MD, PhD is a Professor of Pediatrics and Emergency Medicine at Albert Einstein College of Medicine, Bronx, NY

Richard Evans III, MD, MPH is the is head of the Division of Allergy for Children`s Memorial Hospital and a professor of clinical pediatrics and medicine at Northwestern University Medical School, Chicago, IL

Rebecca S. Gruchalla, MD, PhD is a Professor of Internal Medicine and Pediatrics and Director of the Division of Allergy and Immunology and holds the William A. Sellars M.D. and Joyce M. Sellars Distinguished Chair in Allergy and Immunology at U.T. Southwestern Medical Center, Dallas, TX

Meyer Kattan, MD, CM is a Professor of Pediatrics at Columbia University and the Director of the Pediatric Pulmonary Division at the Children's Hospital of New York, NY. Previously he was Professor of Pediatrics, Chief of the Pediatric Pulmonary and Critical Care Division and Director of the Pediatric Pulmonary Fellowship program at the Mount Sinai School of Medicine in New York, NY

Wayne Morgan, MD, CM is the Associate Director of the Arizona Respiratory Center and a Professor and Section Chief of Pediatrics at the Univ. of Arizona College of Medicine, Tucson, AZ

George T. O'Connor, MD, MS is a Professor of Medicine and the Director of the Adult Asthma Program at Boston Univ. School of Medicine, Boston, MA

James W. Stout, MD, MPH is a Professor of Pediatrics at the Univ. of Washington School of Medicine and Adjunct Professor of Health Services at the University of Washington School of Public Health, Seattle, WA

Herman Mitchell, PhD is Vice President and Senior Research Scientist at Rho Federal Systems Division and an Adjunct Professor of Biostatistics at UNC Gillings School of Global Public Health, Chapel Hill, NC. Dr. Mitchell has served as a Principal Investigator in coordinating some of the largest clinical research projects ever awarded by the NIH.

Appendix B: ICAS Publications

Differential effects of outdoor versus indoor fungal spores on asthma morbidity in inner-city children. Pongracic JA, O'Connor GT, Muilenberg ML, Vaughn B, Gold DR, Kattan M, Morgan WJ, Gruchalla RS, Smartt E, Mitchell HE. J Allergy Clin Immunol. 2010 Mar;125(3):593-9. Epub 2010 Feb 4.

Effect of mouse allergen and rodent environmental intervention on asthma in inner-city children. Pongracic JA, Visness CM, Gruchalla RS, Evans R 3rd, Mitchell HE. Ann Allergy Asthma Immunol. 2008 Jul;101(1):35-41.

Classification of asthma severity in children: the contribution of pulmonary function testing. Stout JW, Visness CM, Enright P, Lamm C, Shapiro G, Gan VN, Adams GK 3rd, Mitchell HE. Arch Pediatr Adolesc Med. 2006 Aug;160(8):844-50.

A randomized clinical trial of clinician feedback to improve quality of care for inner-city children with asthma. Kattan M, Crain EF, Steinbach S, Visness CM, Walter M, Stout JW, Evans R 3rd, Smartt E, Gruchalla RS, Morgan WJ, O'Connor GT, Mitchell HE. Pediatrics. 2006 Jun;117(6):e1095-103.

Cost-effectiveness of a home-based environmental intervention for inner-city children with asthma. Kattan M, Stearns SC, Crain EF, Stout JW, Gergen PJ, Evans R 3rd, Visness CM, Gruchalla RS, Morgan WJ, O'Connor GT, Mastin JP, Mitchell HE. J Allergy Clin Immunol. 2005 Nov;116(5):1058-63. Epub 2005 Oct 3.

Inner City Asthma Study: relationships among sensitivity, allergen exposure, and asthma morbidity. Gruchalla RS, Pongracic J, Plaut M, Evans R 3rd, Visness CM, Walter M, Crain EF, Kattan M, Morgan WJ, Steinbach S, Stout J, Malindzak G, Smartt E, Mitchell H. J Allergy Clin Immunol. 2005 Mar;115(3):478-85.

Airborne fungi in the homes of children with asthma in low-income urban communities: The Inner-City Asthma Study. O'connor GT, Walter M, Mitchell H, Kattan M, Morgan WJ, Gruchalla RS, Pongracic JA, Smartt E, Stout JW, Evans R, Crain EF, Burge HA. J Allergy Clin Immunol. 2004 Sep;114(3):599-606.

Results of a home-based environmental intervention among urban children with asthma. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R 3rd, Stout J, Malindzak G, Smartt E, Plaut M, Walter M, Vaughn B, Mitchell H; Inner-City Asthma Study Group. N Engl J Med. 2004 Sep 9;351(11):1068-80.

Community violence and asthma morbidity: the Inner-City Asthma Study. Wright RJ, Mitchell H, Visness CM, Cohen S, Stout J, Evans R, Gold DR. Am J Public Health. 2004 Apr;94(4):625-32.

Particle concentrations in inner-city homes of children with asthma: the effect of smoking, cooking, and outdoor pollution. Wallace LA, Mitchell H, O'Connor GT, Neas L, Lippmann M, Kattan M, Koenig J, Stout JW, Vaughn BJ, Wallace D, Walter M, Adams K, Liu LJ; Inner-City Asthma Study. Environ Health Perspect. 2003 Jul;111(9):1265-72.

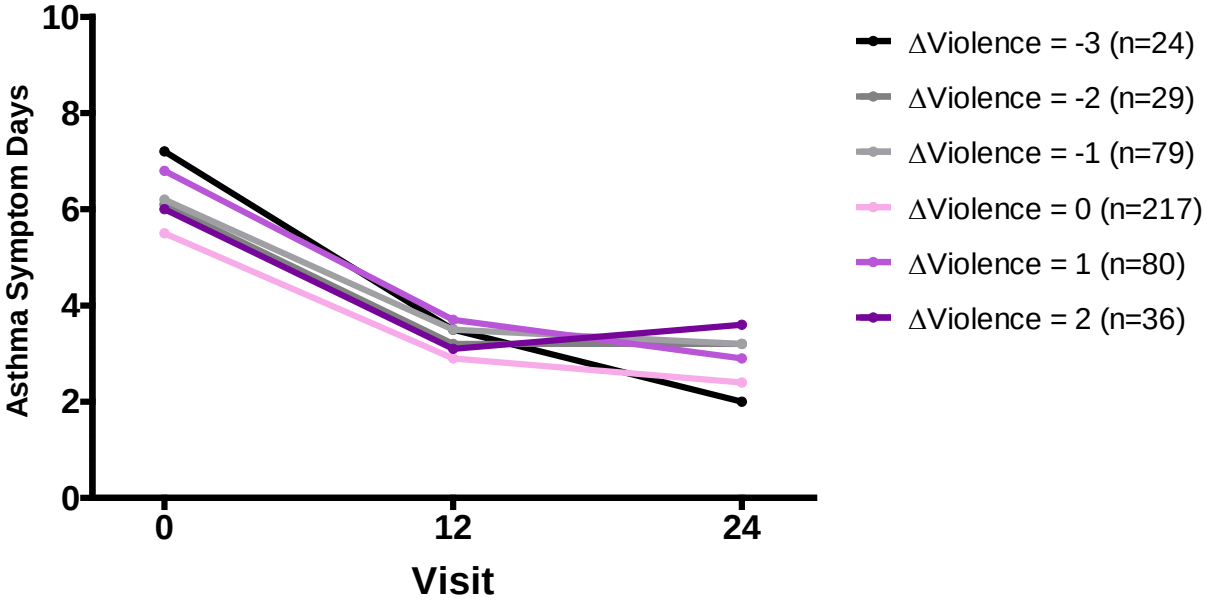
Home and allergic characteristics of children with asthma in seven U.S. urban communities and design of an environmental intervention: the Inner-City Asthma

Study. Crain EF, Walter M, O'Connor GT, Mitchell H, Gruchalla RS, Kattan M, Malindzak GS, Enright P, Evans R 3rd, Morgan W, Stout JW. Environ Health Perspect. 2002 Sep;110(9):939-45.

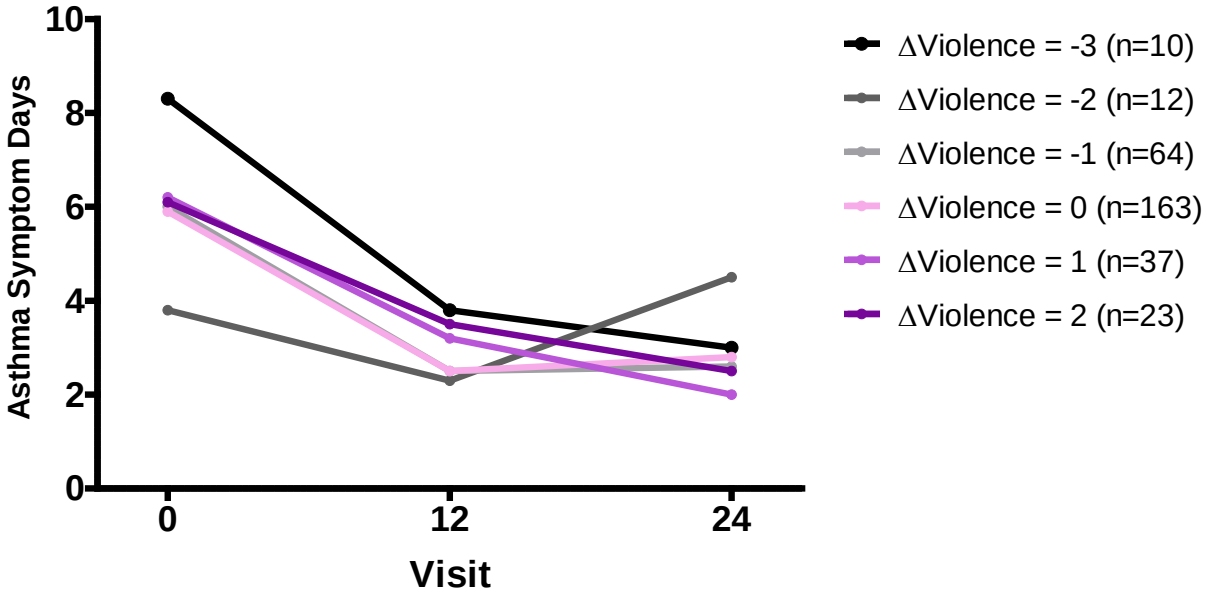
Appendix C: Change in Violence Exposure and Asthma Morbidity

Change in asthma symptom days after a change in violence exposure (measured at 12 months) among asthmatic children sensitized (panel A) and not sensitized (panel B) to cockroach allergen.

A



B



Appendix D: Stress Questionnaire

The questions in the scale ask you about your feelings and thoughts during the last month. In each case, please indicate by circling the number how often you felt or thought a certain way.

[USE HANDCARD IF NOT SELF-ADMINISTERED.]

B1. In the last month, how often have you felt that you were unable to control the important things in your life?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B2. In the last month, how often have you felt confident about your ability to handle your personal problems?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B3. In the last month, how often have you felt that things were going your way?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B4. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

Appendix E: Negative Life Events Questionnaire

I am going to ask you questions about a number of events that commonly happen in people's lives. Each question is concerned with whether an event has happened to you (and in some cases your spouse) during the last 12 months. Please respond "yes" if the event happened and "no" if it didn't. For several of the events, there are also some follow-up questions for those who answer "yes." When I ask a question about your spouse/partner, I am referring to both married spouses and to unmarried partners who live together and have a marital-like relationship.

Some of the questions I will ask may remind you of rather painful feelings. They are, however, extremely important to people when they do happen, so please try to answer.

[If possible, this form should be self-administered. Use handcards if it is not self-administered.]

B1. Have you moved during the last 12 months?

Yes 1
No 0
[SKIP TO B2]

B1a. Overall, would you say that your moving was a good or bad experience?

Very good . . . . . 1 **[SKIP TO B2]**
Moderately good . . . . . 2 **[SKIP TO B2]**
Slightly good . . . . . 3 **[SKIP TO B2]**
Slightly bad 4
Moderately bad 5
Very bad 6

B1a1. In the last month, how often did you experience <u>unwanted</u> thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B2. Have you broken off an engagement to be married or ended an intimate relationship during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B3]**

B2a. How would you rate your feelings about breaking up?

Very good 1	**[SKIP TO B3]**
Moderately good 2	**[SKIP TO B3]**
Slightly good 3	**[SKIP TO B3]**
Slightly bad 4	
Moderately bad 5	
Very bad 6	

B2a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B3. Did you get married during the last 12 months?

Yes 1	
No 0	**[SKIP TO B4]**

B3a. Overall, would you rate getting married as a good or bad experience?

Very good 1	**[SKIP TO B4]**
Moderately good 2	**[SKIP TO B4]**
Slightly good 3	**[SKIP TO B4]**
Slightly bad 4	
Moderately bad 5	
Very bad 6	

B3a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B4. Did someone you were close to die during the last 12 months?

Yes 1
No 0
[SKIP TO B5]

B4a. Who?
[More than one response is possible.]

		Yes=1, No=0
B4a1.	Spouse or Intimate Friend	_____
B4a2.	Parent	_____
B4a3.	Spouse's Parent	_____
B4a4.	Brother or Sister	_____
B4a5.	Child	_____
B4a6.	Other Relatives	_____
B4a7.	Friend	_____
B4a8.	Other	_____

B4a8a. **Specify**: _____

B4b. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B5. Were you separated or divorced during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B6]**

B5a. Overall, would you rate your separation or divorce as a good or bad experience?

Very good . . . . . 1 **[SKIP TO B6]**
Moderately good . . . . . 2 **[SKIP TO B6]**
Slightly good . . . . . 3 **[SKIP TO B6]**
Slightly bad 4
Moderately bad 5
Very bad 6

B5a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B6. Did you break up with a close friend during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B7]**

B6a. Overall, would you rate breaking up as a good or bad experience?

Very good . . . . . 1 **[SKIP TO B7]**
Moderately good . . . . . 2 **[SKIP TO B7]**
Slightly good . . . . . 3 **[SKIP TO B7]**
Slightly bad 4
Moderately bad 5
Very bad 6

B6a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B7. Have you had any important relationship, for. example, with your spouse, a close friend, your boss, or a family member become significantly worse during the last 12 months?
[This should not include the relationship referred to in item 6 above.]

Yes 1
No . . . . . 0 **[SKIP TO B8]**

B7a. With whom?
[More than one response is possible.]

		Yes=1, No=0
B7a1.	Boss	_____
B7a2.	Spouse/Partner	_____
B7a3.	Friend	_____
B7a4.	Child	_____
B7a5.	Parent	_____
B7a6.	Other Family Member	_____

B7a6a. **Specify**: _____

B7b. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B8. Did you have a child or adopt a child during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B9]**

B8a. Overall, would you rate having a child and adjusting to having a child as a good or bad experience?

Very good . . . . . 1 **[SKIP TO B9]**
Moderately good . . . . . 2 **[SKIP TO B9]**
Slightly good . . . . . 3 **[SKIP TO B9]**
Slightly bad 4
Moderately bad 5
Very bad 6

B8a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B9. Have you, a very close friend, or close family member had an accident that required emergency medical treatment during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B10]**

B9a. Who?
[More than one response is possible.]

		Yes=1, No=0
B9a1.	You	_____
B9a2.	Spouse/Partner	_____
B9a3.	Child	_____
B9a4.	Parent	_____
B9a5.	Spouse's Parent	_____
B9a6.	Brother or Sister	_____
B9a7.	Friend	_____
B9a8.	Other	_____

B9a8a. **Specify**_____

B9b. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B10. Have you, a very close friend, or close family member been hospitalized for a serious (life threatening) illness during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B11]**

B10a. Who?
[More than one response is possible.]

	Yes=1, No=0
B10a1. You	_____
B10a2. Spouse/Partner	_____
B10a3. Child	_____
B10a4. Parent	_____
B10a5. Spouse's Parent	_____
B10a6. Brother or Sister	_____
B10a7. Friend	_____
B10a8. Other	_____

B10a8a. **Specify**_____

B10b. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B11. **[TO BE ANSWERED BY INTERVIEWER.]**
What is the gender of the respondent?

Female 0
Male . . . . . 1 **[SKIP TO B11b]**

B11a. **[Ask a WOMAN respondent only.]** Have you been pregnant during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B14]**

B11a1. How would you rate being pregnant?

Very good 1	**[SKIP TO B12a]**
Moderately good 2	**[SKIP TO B12a]**
Slightly good 3	**[SKIP TO B12a]**
Slightly bad 4	
Moderately bad 5	
Very bad 6	

B11a1a. In the last month, how often did you experience <u>unwanted</u> thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . . 3
Very often . . . 4
[SKIP TO B12a]

B11b. **[Ask a MAN respondent only.]** Has your wife, partner or girlfriend been pregnant during the last 12 months?
[Answer "no" if you do not have a wife, partner, or girlfriend.]

Yes 1	
No 0	**[SKIP TO B14]**

B11b1. How do you feel about the pregnancy?

Very good 1	**[SKIP TO B12b]**
Moderately good 2	**[SKIP TO B12b]**
Slightly good 3	**[SKIP TO B12b]**
Slightly bad 4	
Moderately bad 5	
Very bad 6	

B11b1a. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . . 3
Very often . . . 4

[SKIP TO B12b]

B12. **If the respondent is a WOMAN, ask question B12a. If the respondent is a MAN, skip to question B12b.**

B12a. **[Ask a WOMAN respondent only].** Have you had an abortion during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B13a]**

B12a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

[SKIP TO B13a]

B12b. **[Ask a MAN respondent only].** Has your wife, partner or girlfriend had an abortion during the last 12 months?
[Answer "no" if you do not have a wife, partner, or girlfriend.]

Yes 1
No . . . . . 0 **[SKIP TO B13b]**

B12b1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4 **[SKIP TO B13b]**

B13. **If the respondent is a WOMAN, ask question B13a. If the respondent is a MAN, skip to question B13b.**

B13a. **[Ask a WOMAN respondent only].** Have you had a miscarriage or stillbirth during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B14]**

B13a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

[SKIP TO B14]

B13b. **[Ask a MAN respondent only].** Has your wife, partner or girlfriend had a miscarriage or stillbirth during the last 12 months?
[Answer "no" if you do not have a wife, partner, or girlfriend.]

Yes 1
No . . . . . 0 **[SKIP TO B14]**

B13b1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B14. Have you or your spouse/partner lost or changed jobs or been involuntarily unemployed during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B15]**

B14a.How would you rate your feelings about leaving your job (or your spouse leaving his/her job)?

Very good 1	**[SKIP TO B15]**
Moderately good 2	**[SKIP TO B15]**
Slightly good 3	**[SKIP TO B15]**
Slightly bad 4	
Moderately bad 5	
Very bad 6	

B14a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B15. During the last 12 months, have you or your spouse/partner suffered a significant business or investment loss or has a business you owned failed?

Yes 1	
No 0	**[SKIP TO B16]**

B15a. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B16. During the last 12 months, have you or your spouse/partner had any serious problems or disappointment at work or in an educational course (university, training program, etc.)? **[Answer only for you if both had disappointments.]**

Yes 1	
No 0	**[SKIP TO B17]**

B16a In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B17. Have you or your spouse/partner had significant success at work or in an educational course (university, training program, etc.) during last 12 months?

Yes 1
No 0

B18. Has there been a significant change in your personal finances during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B19]**

B18a. Has the change been for the better or worse?

Better . . . . . 1 **[SKIP TO B19]**
Worse 0

B18a1. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B19. Has your house been broken into and/or burglarized during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B20]**

B19a. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B20. Have you or your spouse/partner or other member of your immediate family been assaulted or mugged during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B21]**

B20a. Who?
[More than one response is possible.]

	Yes =1, No= 0
B20a1. You	_____
B20a2. Spouse/Partner	_____
B20a3. Child	_____
B20a4. Parent	_____
B20a5. Brother or Sister	_____
B20a6. Other	_____

B20a6a. **Specify**_____

B20b. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B21. Has the behavior of any member of your family been a significant problem for you during the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO B22]**

B21a. Who?
[More than one response is possible.]

	Yes=1, No=0
B21a1. You	_____
B21a2. Spouse/Partner	_____
B21a3. Child	_____
B21a4. Parent	_____
B21a5. Brother or Sister	_____
B21a6. Other	_____

B21a6a. **Specify**_____

B21b. In the last month, how often did you experience unwanted thoughts, memories, or images about this event?

Never 0
Almost never 1
Sometimes 2
Fairly often 3
Very often 4

B22. Have you or your spouse/partner had to appear in court during the last 12 months as either a defendant, a witness in a criminal case, or as party to a suit?

Yes 1
No . . . . . 0 **[SKIP TO B23]**

B22a. How would you rate the court experience?

Very good 1	**[SKIP TO B23]**
Moderately good 2	**[SKIP TO B23]**
Slightly good 3	**[SKIP TO B23]**
Slightly bad 4	
Moderately bad 5	
Very bad 6	

B22a1. In the last month, how often did you experience <u>unwanted</u> thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B23. Have you had a pet (animal) to whom you were attached die, or get lost, or did you have to give it away during the last 12 month?

Yes 1
No . . . . . 0 **[SKIP TO B24]**

B23a. In the last month, how often did you experience <u>unwanted</u> thoughts, memories, or images about this event?

Never 0
Almost never . 1
Sometimes . . . 2
Fairly often . . 3
Very often . . . 4

B24. Other than the events we have already asked about, have any other important things happened to you or to a very close friend or close family member in the last 12 months that made that period significantly different from a typical year?
[If yes, you can list up to three events. Please do <u>not</u> feel obliged to include an additional event or events unless they were significant.]

Yes 1
No . . . . . 0 **[SKIP TO NEXT FORM]**

B24a. **Event 1**: To whom? **[Only ONE response is possible.]**

You 1
Spouse/Partner 2
Child 3
Parent 4
Brother/Sister 5
Other 6

B24a1. **Specify**_____

B24a2. What happened?_____

_____

B24a3. How would you rate your feelings about this event?

Very good 1
Moderately good 2
Slightly good 3
Slightly bad 4
Moderately bad 5
Very bad 6

B24b. **Event 2**: Has there been another important event in the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO NEXT FORM]**

B24b1. To whom?
[Only ONE response is possible.]

You 1
Spouse/Partner 2
Child 3
Parent 4
Brother/Sister 5
Other 6

B24b1a. **Specify**_____

B24b1b. What happened?_____

B24b1c. How would you rate your feelings about this event?

Very good 1
Moderately good 2
Slightly good 3
Slightly bad 4
Moderately bad 5
Very bad 6

B24c. **Event 3**: Has there been another important event in the last 12 months?

Yes 1
No . . . . . 0 **[SKIP TO NEXT FORM]**

B24c1. To whom?
[Only ONE response is possible.]

You 1
Spouse/Partner 2
Child 3
Parent 4
Brother/Sister 5
Other 6

B24c1a. **Specify**_____

B24c1b. What happened?_____

_____

B24c1c. How would you rate your feelings about this event?

Very good 1
Moderately good 2
Slightly good 3
Slightly bad 4
Moderately bad 5
Very bad 6

Appendix F: Medication Adherence Questionnaire

Many families have problems making sure children get all of their asthma medications or making sure they get medicines on time. I am going to go over several areas and ask whether this has been hard for you.

[VERIFY THAT CHILD HAS TAKEN MEDS FOR ASTHMA IN THE PAST 6 MONTHS. IF CHILD HAS NOT, ASK ONLY B3, B9, B12, B13. THESE QUESTION NUMBERS ARE HIGHLIGHTED. ENTER "-1" FOR ALL OTHER QUESTIONS.]

B1. Many families have problems getting the medicines their child needs because the pharmacy does not have the medicine or it is hard to get to the pharmacy.

In the past 6 months, have you had any problems like these when trying to get [CHILD] his/her asthma medicines?

Yes	1	
No	0	**[SKIP TO B2]**
N/A	-1	**[SKIP TO B2]**

B1a. In the past 6 months, have you had to skip some of [CHILD]'s medicine because of problems like these?

Yes	1
No	0

B2. Some families have problems getting their child's asthma medicines because they do not have insurance and the medicines cost too much.

In the past 6 months, have you had any problems trying to get [CHILD] his/her asthma medicine because of financial problems like these?

Yes	1	
No	0	**[SKIP TO B3]**
N/A	-1	**[SKIP TO B3]**

B2a. Have you had to skip some of [CHILD]'s medicines because of these problems?

Yes	1
No	0

B3. In the past 6 months, have you <u>ever</u> run out of medicines for [CHILD]'s asthma and not had any when
[CHILD] had an asthma attack?

Yes	1
No	0

B4. Sometimes families have trouble giving asthma medicines because the child refuses to take the medicine. Sometimes it's because the child is too busy playing or the medicine tastes bad or makes him/her feel funny.

In the past 6 months, has this ever been a problem in your family?

Yes	1	
No	0	**[SKIP TO B5]**
N/A	-1	**[SKIP TO B5]**

B4a. Have you had to skip a dose of medicine because of this problem?

Yes	1
No	0

B5. Asthma medication schedules can be hard to follow. When there are many medicines to keep track of, the schedule can be hard.

Do you feel that [CHILD]'s medication schedule is hard to follow?

Yes	1	
No	0	**[SKIP TO B6]**
N/A	-1	**[SKIP TO B6]**

B5a. Are there times you have had problems giving [CHILD] his/her medications and ended up skipping a dose?

Yes	1
No	0

B6. Some families do not give their child all the asthma medicine prescribed by the doctor because they feel that he/she could become addicted or that too much medicine is bad. Other times, it may be that the child or the adults in the home do not like the side effects.

Do you feel [CHILD] is getting too much, too little, or just the right amount of medicine?

Too much	1	
Too little	2	
Right amount	3	**[ASK B6a, THEN SKIP TO B7]**
N/A	-1	

B6a. In the past 6 months, have you worried about any of the side effects from [CHILD]'s asthma medications?

Yes	1	
No	0	**[SKIP TO B7]**
N/A	-1	**[SKIP TO B7]**

B6b. In the past 6 months, have you ever cut back on [CHILD]'s asthma medications because of these worries?

Yes 1
No 0

B7. There are times when people think the child is all better before finishing the prescription. In the past 6 months, have you thought [CHILD]'s asthma was better before finishing the prescription?

Yes 1
No . . . . . 0 **[SKIP TO B8]**
N/A . . . . . -1 **[SKIP TO B8]**

B7a. Did you stop using the medicine because [CHILD] felt better?

Yes 1
No 0

B8. Some families feel that the asthma medications do not really work. In the past 6 months, have you felt this way?

Yes 1
No . . . . . 0 **[SKIP TO B9]**
N/A . . . . . -1 **[SKIP TO B9]**

B8a. Are there times you stopped giving [CHILD] the asthma medicines because you felt this way?

Yes 1
No 0

B9. Sometimes family or friends recommend using remedies such as teas, rubs, and herbs for asthma.
In the past 6 months, have you used any remedies recommended by a friend or relative?

Yes 1
No . . . . . 0 **[SKIP TO B10]**

B9a. Did you use these instead of [CHILD]'s regular asthma medication?

Yes 1
No 0

B10. **[USE HANDCARD]** For many other reasons, children do not always get their medicines exactly when they are supposed to.

On a scale of 1 to 5, [1 is no problems and 5 is a lot of problems with medicines] how many problems do you usually face when trying to be sure [CHILD] gets his/her medicines?

-1	1	2	3	4	5
N/A	No problem				A lot of problems

B11. **[USE HANDCARD]** On a scale of 1 to 5, [1 means never missing a dose of medicine and 5 means often missing a dose] how would you rate [CHILD]'s experience with taking his/her medicines exactly on schedule?

-1	1	2	3	4	5
N/A	Never misses a dose				Often misses a dose

B12. Many people have problems making and keeping doctor's appointments for their child's asthma. Sometimes appointments are hard to get or people have to wait a long time. Sometimes it is hard to get to the office or they are not open at good times.

In the past 6 months, have you had any problems making or keeping appointments for [CHILD]'s asthma?

Yes 1
No . . . . . 0 **[SKIP TO B13]**

B12a. In the past 6 months, have you missed any appointments or chosen not to make one because of these problems?

Yes 1
No 0

B13. Many people have problems making or keeping appointments because they can not afford the cost of the appointment or because of problems with insurance.

In the 6 months, have you had any financial or insurance problems with making or keeping [CHILD]'s appointments?

Yes 1
No . . . . . 0 **[SKIP TO NEXT FORM]**

B13a. In the past 6 months, have you missed any appointments or chosen not to make one because of money or insurance problems?

Yes 1
No 0

Appendix G: Violence Score Table

	Violence score	0	1	2	3	4	5	Chi Square p-value
Afraid to Play Outside	No	344	143	65	47	12	6	<0.001
	Yes	105	70	61	51	21	9	
Exp + Sens to Cockroach	No	324	155	73	58	19	6	<0.001
	Yes	108	48	47	38	14	7	
Sensitized to Cockroach	No	190	98	37	32	10	5	0.006
	Yes	258	115	89	66	23	10	
Exposed to Cockroach	No	289	125	62	49	16	6	<0.001
	Yes	144	78	58	47	17	7	
Black	No	286	122	72	55	16	9	0.30
	Yes	163	91	54	43	17	6	
Hispanic	No	240	130	73	63	21	9	0.26
	Yes	209	83	53	35	12	6	
Site	Boston	56	32	17	10	2	1	<0.001
	Bronx	58	26	26	16	5	2	
	Chicago	58	29	20	21	10	3	
	Dallas	68	38	17	8	2	2	
	New York	54	27	21	23	11	5	
	Seattle	64	40	11	9	2	1	
	Tucson	91	21	14	11	1	1	
Ever Skip Meds	No	301	144	77	49	19	8	0.02
	Yes	143	68	48	48	14	7	
Smoker in home	No	242	110	64	47	15	5	0.55
	Yes	207	103	62	51	18	10	
Income	< $15,000	171	89	44	30	13	4	0.34
	≥ $15,000	247	115	74	67	20	10	
Caretaker Completed HS	No	142	63	35	28	10	4	0.96
	Yes	305	147	91	68	22	11	
Employed in Household	None	89	51	33	27	17	6	<0.001
	1 or more	357	162	92	71	16	9	
Home Problems and Deterioration Score	0	207	87	49	37	5	6	0.07
	1	135	75	40	33	15	3	
	2	40	13	11	13	6	3	
	3	23	16	15	6	3	2	
	4	15	13	5	5	2	0	

	Violence score	0	1	2	3	4	5	Chi Square p-value
	5	16	3	0	2	1	1	
	6	13	6	6	2	1	0	
Stress Score	0	38	13	6	4	0	0	0.14
	1	32	14	5	0	1	0	
	2	32	17	8	10	4	1	
	3	35	19	6	4	1	2	
	4	53	24	15	10	5	3	
	5	28	19	8	9	2	0	
	6	51	27	17	11	5	1	
	7	60	20	16	12	3	0	
	8	54	19	13	13	5	2	
	9	32	14	15	9	2	0	
	10	17	12	6	4	4	3	
	11	9	6	5	5	0	1	
	12+	6	8	6	6	1	2	
Max # of unwanted thoughts	0	195	58	39	23	5	3	<0.001
	1	30	15	4	3	3	0	
	2	100	49	26	25	9	1	
	3	60	43	24	12	4	1	
	4	59	45	32	35	12	10	
# of Negative Life Events	0	133	42	28	13	2	3	<0.001
	1	108	39	22	21	5	0	
	2	75	36	17	12	4	0	
	3	44	27	14	13	7	3	
	4	24	24	17	16	3	0	
	5	23	17	7	6	1	1	
	6	13	6	9	5	6	1	
	7	9	7	5	2	1	4	
	8	8	8	1	2	1	0	
	9	4	2	4	2	1	1	
	10+	6	4	2	6	2	2	
Asthma Symptom Days		5.6	5.9	6.2	6.6	7.6	9.7	<0.01

References

1. Contopoulos-Ioannidis DG, Kouri IN, Ioannidis JP. Genetic predisposition to asthma and atopy. *Respiration.* 2007;74(1):8-12.

2. Cohn RD, Arbes SJ, Jr., Yin M, Jaramillo R, Zeldin DC. National prevalence and exposure risk for mouse allergen in US households. *J Allergy Clin Immunol.* Jun 2004;113(6):1167-1171.

3. Bloom B, Cohen RA, Freeman G. Summary health statistics for U.S. children: National Health Interview Survey, 2008. *Vital and health statistics. Series 10, Data from the National Health Survey.* 2009 Dec 2009(244):1-81.

4. Pleis J, Lucas J, Ward B. Summary health statistics for U.S. adults: National Health Interview Survey, 2008. *Vital and health statistics. Series 10, Data from the National Health Survey.* 2009(242).

5. Lara M, Akinbami L, Flores G, Morgenstern H. Heterogeneity of childhood asthma among Hispanic children: Puerto Rican children bear a disproportionate burden. *Pediatrics.* Jan 2006;117(1):43-53.

6. Cherry DK, Hing E, Woodwell DA, Rechtsteiner EA. National Ambulatory Medical Care Survey: 2006 summary. *Natl Health Stat Report.* Aug 6 2008(3):1-39.

7. Hing E, Hall MJ, Xu J. National Hospital Ambulatory Medical Care Survey: 2006 outpatient department summary. *Natl Health Stat Report.* Aug 6 2008(4):1-31.

8. Pitts SR, Niska RW, Xu J, Burt CW. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Natl Health Stat Report.* Aug 6 2008(7):1-38.

9. National Heart L, and Blood Institute. Morbidity & Mortality: 2009 Chart Book on Cardiovascular, Lung, and Blood Diseases. Bethesda, MD: National Institutes of Health; 2009.

10. Heron M, Sutton PD, Xu J, Ventura SJ, Strobino DM, Guyer B. Annual summary of vital statistics: 2007. *Pediatrics.* Jan 2010;125(1):4-15.

11. Arshad SH, Tariq SM, Matthews S, Hakim E. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. *Pediatrics.* Aug 2001;108(2):E33.

12. Call RS, Smith TF, Morris E, Chapman MD, Platts-Mills TA. Risk factors for asthma in inner city children. *J Pediatr.* Dec 1992;121(6):862-866.

13. Ingram JM, Sporik R, Rose G, Honsinger R, Chapman MD, Platts-Mills TA. Quantitative assessment of exposure to dog (Can f 1) and cat (Fel d 1) allergens: relation to sensitization and asthma among children living in Los Alamos, New Mexico. *J Allergy Clin Immunol.* Oct 1995;96(4):449-456.

14. Nelson RP, Jr., DiNicolo R, Fernandez-Caldas E, Seleznick MJ, Lockey RF, Good RA. Allergen-specific IgE levels and mite allergen exposure in children with acute asthma first seen in an emergency department and in nonasthmatic control subjects. *J Allergy Clin Immunol.* Aug 1996;98(2):258-263.

15. Platts-Mills TA, Vervloet D, Thomas WR, Aalberse RC, Chapman MD. Indoor allergens and asthma: report of the Third International Workshop. *J Allergy Clin Immunol.* Dec 1997;100(6 Pt 1):S2-24.

16. Pollart SM, Smith TF, Morris EC, Gelber LE, Platts-Mills TA, Chapman MD. Environmental exposure to cockroach allergens: analysis with monoclonal antibody-based enzyme immunoassays. *J Allergy Clin Immunol.* Feb 1991;87(2):505-510.

17. Sears MR, Herbison GP, Holdaway MD, Hewitt CJ, Flannery EM, Silva PA. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. *Clin Exp Allergy.* Jul 1989;19(4):419-424.

18. Squillace SP, Sporik RB, Rakes G, et al. Sensitization to dust mites as a dominant risk factor for asthma among adolescents living in central Virginia. Multiple regression analysis of a population-based study. *Am J Respir Crit Care Med.* Dec 1997;156(6):1760-1764.

19. Gruchalla RS, Pongracic J, Plaut M, et al. Inner City Asthma Study: relationships among sensitivity, allergen exposure, and asthma morbidity. *J Allergy Clin Immunol.* Mar 2005;115(3):478-485.

20. Gergen PJ, Arbes SJ, Jr., Calatroni A, Mitchell HE, Zeldin DC. Total IgE levels and asthma prevalence in the US population: results from the National Health and Nutrition Examination Survey 2005-2006. *J Allergy Clin Immunol.* 2009 Sep 2009;124(3):447-453.

21. Arbes SJ, Jr., Gergen PJ, Elliott L, Zeldin DC. Prevalences of positive skin test responses to 10 common allergens in the US population: results from the third National Health and Nutrition Examination Survey. *J Allergy Clin Immunol.* Aug 2005;116(2):377-383.

22. Cohn RD, Arbes SJ, Jr., Jaramillo R, Reid LH, Zeldin DC. National prevalence and exposure risk for cockroach allergen in U.S. households. *Environ Health Perspect.* Apr 2006;114(4):522-526.

23. Arbes SJ, Jr., Cohn RD, Yin M, et al. House dust mite allergen in US beds: results from the First National Survey of Lead and Allergens in Housing. *J Allergy Clin Immunol.* Feb 2003;111(2):408-414.

24. Arbes SJ, Jr., Cohn RD, Yin M, Muilenberg ML, Friedman W, Zeldin DC. Dog allergen (Can f 1) and cat allergen (Fel d 1) in US homes: results from the National Survey of Lead and Allergens in Housing. *J Allergy Clin Immunol.* Jul 2004;114(1):111-117.

25. Celedon JC, Milton DK, Ramsey CD, et al. Exposure to dust mite allergen and endotoxin in early life and asthma and atopy in childhood. *J Allergy Clin Immunol.* Jul 2007;120(1):144-149.

26. Arruda LK, Vailes LD, Ferriani VP, Santos AB, Pomes A, Chapman MD. Cockroach allergens and asthma. *J Allergy Clin Immunol.* Mar 2001;107(3):419-428.

27. Gelber LE, Seltzer LH, Bouzoukis JK, Pollart SM, Chapman MD, Platts-Mills TA. Sensitization and exposure to indoor allergens as risk factors for asthma among patients presenting to hospital. *Am Rev Respir Dis.* Mar 1993;147(3):573-578.

28. Eggleston PA, Rosenstreich D, Lynn H, et al. Relationship of indoor allergen exposure to skin test sensitivity in inner-city children with asthma. *The Journal of allergy and clinical immunology.* 1998 Oct 1998;102(4 Pt 1):563-570.

29. Huss K, Adkinson NF, Jr., Eggleston PA, Dawson C, Van Natta ML, Hamilton RG. House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Childhood Asthma Management Program. *J Allergy Clin Immunol.* Jan 2001;107(1):48-54.

30. Rosenfeld L, Rudd R, Chew GL, Emmons K, Acevedo-Garcia D. Are neighborhood-level characteristics associated with indoor allergens in the household? *J Asthma.* 2010 Feb 2010;47(1):66-75.

31. Sarpong SB, Hamilton RG, Eggleston PA, Adkinson NF, Jr. Socioeconomic status and race as risk factors for cockroach allergen exposure and sensitization in children with asthma. *J Allergy Clin Immunol.* Jun 1996;97(6):1393-1401.

32. Tepas EC, Litonjua AA, Celedon JC, Sredl D, Gold DR. Sensitization to aeroallergens and airway hyperresponsiveness at 7 years of age. *Chest.* Jun 2006;129(6):1500-1508.

33. Erwin EA, Wickens K, Custis NJ, et al. Cat and dust mite sensitivity and tolerance in relation to wheezing among children raised with high exposure to both allergens. *J Allergy Clin Immunol.* Jan 2005;115(1):74-79.

34. Rosenstreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med.* May 8 1997;336(19):1356-1363.

35. Litonjua AA, Carey VJ, Burge HA, Weiss ST, Gold DR. Exposure to cockroach allergen in the home is associated with incident doctor-diagnosed asthma and recurrent wheezing. *J Allergy Clin Immunol.* Jan 2001;107(1):41-47.

36. Association AL. Urban air pollution and health inequities: a workshop report. *Environ Health Perspect.* Jun 2001;109 Suppl 3:357-374.

37. Mosges R, Klimek L. Today's allergic rhinitis patients are different: new factors that may play a role. *Allergy.* Sep 2007;62(9):969-975.

38. Kang BC, Johnson J, Veres-Thorner C. Atopic profile of inner-city asthma with a comparative analysis on the cockroach-sensitive and ragweed-sensitive subgroups. *J Allergy Clin Immunol.* Dec 1993;92(6):802-811.

39. Matsui EC, Hansel NN, McCormack MC, Rusher R, Breysse PN, Diette GB. Asthma in the inner city and the indoor environment. *Immunol Allergy Clin North Am.* Aug 2008;28(3):665-686, x.

40. Crain EF, Walter M, O'Connor GT, et al. Home and allergic characteristics of children with asthma in seven U.S. urban communities and design of an environmental intervention: the Inner-City Asthma Study. *Environ Health Perspect.* Sep 2002;110(9):939-945.

41. Finkelhor D, Turner H, Ormrod R, Hamby SL. Trends in childhood violence and abuse exposure: evidence from 2 national surveys. *Archives of pediatrics & adolescent medicine.* 2010 Mar 2010;164(3):238-242.

42. Berz JB, Carter AS, Wagmiller RL, Horwitz SM, Murdock KK, Briggs-Gowan M. Prevalence and correlates of early onset asthma and wheezing in a healthy birth cohort of 2- to 3-year olds. *Journal of pediatric psychology.* 2007;32(2):154-166.

43. Wright RJ, Steinbach SF. Violence: an unrecognized environmental exposure that may contribute to greater asthma morbidity in high risk inner-city populations. *Environ Health Perspect.* 2001 Oct 2001;109(10):1085-1089.

44. Wright R, Speizer F, Tager I, Hanrahan J. Children's distress and violence exposure: relation to respiratory symptoms, asthma, and behavior [Abstract]. *Am J Respir Crit Care Med.* 1998;157:A41.

45. Apter AJ, Garcia LA, Boyd RC, Wang X, Bogen DK, Ten Have T. Exposure to community violence is associated with asthma hospitalizations and

emergency department visits. *J Allergy Clin Immunol.* Sep 2010;126(3):552-557.

46. Cohen RT, Canino GJ, Bird HR, Celedon JC. Violence, abuse, and asthma in Puerto Rican children. *American journal of respiratory and critical care medicine.* 2008 Sep 1 2008;178(5):453-459.

47. Clougherty JE, Levy JI, Kubzansky LD, et al. Synergistic effects of traffic-related air pollution and exposure to violence on urban asthma etiology. *Environmental health perspectives.* 2007 Aug 2007;115(8):1140-1146.

48. Wright RJ. Health effects of socially toxic neighborhoods: the violence and urban asthma paradigm. *Clinics in chest medicine.* 2006 Sep 2006;27(3):413-421, v.

49. Cooley-Strickland M, Quille TJ, Griffin RS, Stuart EA, Bradshaw CP, Furr-Holden D. Community violence and youth: affect, behavior, substance use, and academics. *Clinical child and family psychology review.* 2009 Jun 2009;12(2):127-156.

50. Fowler PJ, Tompsett CJ, Braciszewski JM, Jacques-Tiura AJ, Baltes BB. Community violence: a meta-analysis on the effect of exposure and mental health outcomes of children and adolescents. *Development and psychopathology.* 2009;21(1):227-259.

51. Howard DE, Feigelman S, Li X, Cross S, Rachuba L. The relationship among violence victimization, witnessing violence, and youth distress. *J Adolesc Health.* 2002 Dec 2002;31(6):455-462.

52. Kelly S. The psychological consequences to adolescents of exposure to gang violence in the community: an integrated review of the literature. *Journal of child and adolescent psychiatric nursing : official publication of the Association of Child and Adolescent Psychiatric Nurses, Inc.* 2010 May 2010;23(2):61-73.

53. Kennedy AC, Bybee D, Sullivan CM, Greeson M. The impact of family and community violence on children's depression trajectories: examining the interactions of violence exposure, family social support, and gender. *Journal of family psychology : JFP : journal of the Division of Family Psychology of the American Psychological Association (Division 43).* 2010 Apr 2010;24(2):197-207.

54. Logsdon MCCINIMHNJ, Pmid. Violence exposure in children, adolescents, and women: the lived experience. *Issues in mental health nursing.* 2010 Jan 2010;31(1):2-3.

55. Mitchell SJ, Lewin A, Horn IB, Valentine D, Sanders-Phillips K, Joseph JG. How does violence exposure affect the psychological health and parenting of

young African-American mothers? *Social science & medicine (1982).* 2010 Feb 2010;70(4):526-533.

56. Wilson WC, Rosenthal BS. The relationship between exposure to community violence and psychological distress among adolescents: a meta-analysis. *Violence and victims.* 2003 Jun 2003;18(3):335-352.

57. Zinzow HM, Ruggiero KJ, Resnick H, et al. Prevalence and mental health correlates of witnessed parental and community violence in a national sample of adolescents. *Journal of child psychology and psychiatry, and allied disciplines.* 2009 Apr 2009;50(4):441-450.

58. Horowitz K, Weine S, Jekel J. PTSD symptoms in urban adolescent girls: compounded community trauma. *J Am Acad Child Adolesc Psychiatry.* Oct 1995;34(10):1353-1361.

59. Martinez P, Richters JE. The NIMH community violence project: II. Children's distress symptoms associated with violence exposure. *Psychiatry.* Feb 1993;56(1):22-35.

60. Pynoos RS, Frederick C, Nader K, et al. Life threat and posttraumatic stress in school-age children. *Arch Gen Psychiatry.* Dec 1987;44(12):1057-1063.

61. Osofsky JD. The impact of violence on children. *Future Child.* Winter 1999;9(3):33-49.

62. Li X, Howard D, Stanton B, Rachuba L, Cross S. Distress symptoms among urban African American children and adolescents: a psychometric evaluation of the Checklist of Children's Distress Symptoms. *Arch Pediatr Adolesc Med.* Jun 1998;152(6):569-577.

63. Federico MJ, Liu AH. Overcoming childhood asthma disparities of the inner-city poor. *Pediatr Clin North Am.* 2003 Jun 2003;50(3):655-675, vii.

64. Holaday B. Images of the neighborhood and activity patterns of chronically ill schoolage children. *Environment and Behavior.* 1997;29(3):348-373.

65. Kalish M, Banco L, Burke G, Lapidus G. Outdoor play: A survey of parent's perceptions of their child's safety. *J Trauma.* 2010;69(4 Suppl):S218-222.

66. Miles R. Neighborhood disorder, perceived safety, and readiness to encourage use of local playgrounds. *Am J Prev Med.* Apr 2008;34(4):275-281.

67. Goodway JD, Smith DW. Keeping all children healthy: challenges to leading an active lifestyle for preschool children qualifying for at-risk programs. *Fam Community Health.* Apr-Jun 2005;28(2):142-155.

68. Gomez JE, Johnson BA, Selva M, Sallis JF. Violent crime and outdoor physical activity among inner-city youth. *Prev Med.* Nov 2004;39(5):876-881.

69. Roman CG, Chalfin A. Fear of walking outdoors. A multilevel ecologic analysis of crime and disorder. *Am J Prev Med.* 2008 Apr 2008;34(4):306-312.

70. Weir LA, Etelson D, Brand DA. Parents' perceptions of neighborhood safety and children's physical activity. *Prev Med.* Sep 2006;43(3):212-217.

71. Roman CG, Knight CR, Chalfin A, Popkin SJ. The relation of the perceived environment to fear, physical activity, and health in public housing developments: evidence from Chicago. *J Public Health Policy.* 2009;30 Suppl 1:S286-308.

72. CDC. Neighborhood safety and the prevalence of physical inactivity--selected states, 1996. *MMWR Morb Mortal Wkly Rep.* Feb 26 1999;48(7):143-146.

73. Burdette HL, Whitaker RC. A national study of neighborhood safety, outdoor play, television viewing, and obesity in preschool children. *Pediatrics.* Sep 2005;116(3):657-662.

74. Mitchell JA, Mattocks C, Ness AR, et al. Sedentary behavior and obesity in a large cohort of children. *Obesity (Silver Spring).* Aug 2009;17(8):1596-1602.

75. Ahmad N, Biswas S, Bae S, Meador KE, Huang R, Singh KP. Association between obesity and asthma in US children and adolescents. *J Asthma.* 2009 Sep 2009;46(7):642-646.

76. Sharp LK, Curtis LM, Mosnaim G, Shalowitz MU, Catrambone C, Sadowski LS. The influence of caregiver's psychosocial status on childhood asthma and obesity. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology.* 2009 Nov 2009;103(5):386-394.

77. Saha C, Riner ME, Liu G. Individual and neighborhood-level factors in predicting asthma. *Arch Pediatr Adolesc Med.* Aug 2005;159(8):759-763.

78. Visness CM, London SJ, Daniels JL, et al. Association of childhood obesity with atopic and nonatopic asthma: results from the National Health and Nutrition Examination Survey 1999-2006. *J Asthma.* Sep 2010;47(7):822-829.

79. Visness CM, London SJ, Daniels JL, et al. Association of obesity with IgE levels and allergy symptoms in children and adolescents: results from the National Health and Nutrition Examination Survey 2005-2006. *J Allergy Clin Immunol.* May 2009;123(5):1163-1169, 1169 e1161-1164.

80. Chilmonczyk BA, Salmun LM, Megathlin KN, et al. Association between exposure to environmental tobacco smoke and exacerbations of asthma in children. *N Engl J Med.* Jun 10 1993;328(23):1665-1669.

81. Mitchell H, Senturia Y, Gergen P, et al. Design and methods of the National Cooperative Inner-City Asthma Study. *Pediatr Pulmonol.* Oct 1997;24(4):237-252.

82. Wright RJ, Subramanian SV. Advancing a multilevel framework for epidemiologic research on asthma disparities. *Chest.* 2007 Nov 2007;132(5 Suppl):757S-769S.

83. Kattan M, Mitchell H, Eggleston P, et al. Characteristics of inner-city children with asthma: the National Cooperative Inner-City Asthma Study. *Pediatr Pulmonol.* Oct 1997;24(4):253-262.

84. Diette GB, Hansel NN, Buckley TJ, et al. Home indoor pollutant exposures among inner-city children with and without asthma. *Environ Health Perspect.* Nov 2007;115(11):1665-1669.

85. Stillman FA, Bone L, Avila-Tang E, et al. Barriers to smoking cessation in inner-city African American young adults. *Am J Public Health.* Aug 2007;97(8):1405-1408.

86. Wood RA, Bloomberg GR, Kattan M, et al. Relationships among environmental exposures, cord blood cytokine responses, allergy, and wheeze at 1 year of age in an inner-city birth cohort (Urban Environment and Childhood Asthma study). *J Allergy Clin Immunol.* Apr 2011;127(4):913-919 e911-916.

87. The health consequences of involuntary exposure to tobacco smoke : a report of the Surgeon General. In: U.S. Dept. of Health and Human Services CfDCaP, Coordinating Center for Health Promotion, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, ed. Atlanta, GA 2006.

88. Samet JM. Secondhand smoke: facts and lies. *Salud Publica Mex.* Sep-Oct 2008;50(5):428-434.

89. Schwartz J, Timonen KL, Pekkanen J. Respiratory effects of environmental tobacco smoke in a panel study of asthmatic and symptomatic children. *Am J Respir Crit Care Med.* Mar 2000;161(3 Pt 1):802-806.

90. Sturm JJ, Yeatts K, Loomis D. Effects of tobacco smoke exposure on asthma prevalence and medical care use in North Carolina middle school children. *Am J Public Health.* Feb 2004;94(2):308-313.

91. Weitzman M, Gortmaker S, Walker DK, Sobol A. Maternal smoking and childhood asthma. *Pediatrics.* Apr 1990;85(4):505-511.

92. Gilliland FD, Berhane K, Islam T, et al. Environmental tobacco smoke and absenteeism related to respiratory illness in schoolchildren. *Am J Epidemiol.* May 15 2003;157(10):861-869.

93. Mannino DM, Homa DM, Redd SC. Involuntary smoking and asthma severity in children: data from the Third National Health and Nutrition Examination Survey. *Chest.* Aug 2002;122(2):409-415.

94. Gerald LB, Gerald JK, Gibson L, Patel K, Zhang S, McClure LA. Changes in environmental tobacco smoke exposure and asthma morbidity among urban school children. *Chest.* Apr 2009;135(4):911-916.

95. McConnell R, Berhane K, Gilliland F, et al. Asthma in exercising children exposed to ozone: a cohort study. *Lancet.* Feb 2 2002;359(9304):386-391.

96. Shima M, Nitta Y, Ando M, Adachi M. Effects of air pollution on the prevalence and incidence of asthma in children. *Arch Environ Health.* Nov-Dec 2002;57(6):529-535.

97. Zmirou D, Gauvin S, Pin I, et al. Traffic related air pollution and incidence of childhood asthma: results of the Vesta case-control study. *J Epidemiol Community Health.* Jan 2004;58(1):18-23.

98. Anderson HR, Ruggles R, Pandey KD, et al. Ambient particulate pollution and the world-wide prevalence of asthma, rhinoconjunctivitis and eczema in children: Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC). *Occup Environ Med.* May;67(5):293-300.

99. Delfino RJ, Staimer N, Tjoa T, et al. Personal and ambient air pollution exposures and lung function decrements in children with asthma. *Environ Health Perspect.* Apr 2008;116(4):550-558.

100. O'Connor GT, Neas L, Vaughn B, et al. Acute respiratory health effects of air pollution on children with asthma in US inner cities. *J Allergy Clin Immunol.* May 2008;121(5):1133-1139 e1131.

101. Hanna AF, Yeatts KB, Xiu A, et al. Associations between ozone and morbidity using the Spatial Synoptic Classification system. *Environ Health.* 2011;10:49.

102. Sexton K, Gong H, Jr., Bailar JC, 3rd, et al. Air pollution health risks: do class and race matter? *Toxicol Ind Health.* Sep-Oct 1993;9(5):843-878.

103. Korc ME. A socioeconomic assessment of human exposure to ozone in the South Coast Air Basin of California. *J Air Waste Manag Assoc.* Jun 1996;46(6):547-557.

104. Morgan WJ, Crain EF, Gruchalla RS, et al. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med.* Sep 9 2004;351(11):1068-1080.

105. Wright RJ, Mitchell H, Visness CM, et al. Community violence and asthma morbidity: the Inner-City Asthma Study. *Am J Public Health.* 2004;94(4):625-632.

106. Peters JL, Suglia SF, Platts-Mills TA, Hosen J, Gold DR, Wright RJ. Relationships among prenatal aeroallergen exposure and maternal and cord blood IgE: project ACCESS. *J Allergy Clin Immunol.* 2009 May 2009;123(5):1041-1046.

107. Richters J MP. Survey of Exposure to Community Violence - Parent Report Version. Bethesda, MD: Child and Adolescent Disorders Research Branch, National Institute of Mental Health; 1990.

108. Thomson CC, Roberts K, Curran A, Ryan L, Wright RJ. Caretaker-child concordance for child's exposure to violence in a preadolescent inner-city population. *Archives of pediatrics & adolescent medicine.* 2002 Aug 2002;156(8):818-823.

109. Sampson RJ, Raudenbush SW, Earls F. Neighborhoods and violent crime: a multilevel study of collective efficacy. *Science.* Aug 15 1997;277(5328):918-924.

110. Peterson RD, and Lauren J. Krivo. National Neighborhood Crime Study (NNCS). Ann Arbor, MI: Inter-University Consortium for Political and Social Research; 2000.

111. Burnham KP, and Anderson, D.R. Multimodel inference: understanding AIC and BIC in Model Selection. *Sociological Methods and Research.* 2004;33(2):261-304.

112. Burnham KP, Anderson, David R. *Model Selection and Multi-Model Inference: A Practical Information-Theoretic Approach*. 2nd ed. New York, NY: Springer; 2002.

113. Trickett PK, Duran L, Horn JL. Community violence as it affects child development: issues of definition. *Clin Child Fam Psychol Rev.* Dec 2003;6(4):223-236.

114. Wright RJ. Epidemiology of stress and asthma: from constricting communities and fragile families to epigenetics. *Immunol Allergy Clin North Am.* Feb 2011;31(1):19-39.

115. Gupta RS, Zhang X, Sharp LK, Shannon JJ, Weiss KB. The protective effect of community factors on childhood asthma. *J Allergy Clin Immunol.* 2009 Jun 2009;123(6):1297-1304.e1292.

116. Gupta RS, Zhang X, Springston EE, et al. The association between community crime and childhood asthma prevalence in Chicago. *Annals of allergy, asthma & immunology : official publication of the American College of Allergy, Asthma, & Immunology.* 2010 Apr 2010;104(4):299-306.

117. Busse WW, Mitchell H. Addressing issues of asthma in inner-city children. *J Allergy Clin Immunol.* Jan 2007;119(1):43-49.

118. Eggleston PA, Butz A, Rand C, et al. Home environmental intervention in inner-city asthma: a randomized controlled clinical trial. *Ann Allergy Asthma Immunol.* Dec 2005;95(6):518-524.

119. Krieger JW, Takaro TK, Song L, Weaver M. The Seattle-King County Healthy Homes Project: a randomized, controlled trial of a community health worker intervention to decrease exposure to indoor asthma triggers. *Am J Public Health.* Apr 2005;95(4):652-659.

120. McConnell R, Milam J, Richardson J, et al. Educational intervention to control cockroach allergen exposure in the homes of hispanic children in Los Angeles: results of the La Casa study. *Clin Exp Allergy.* Apr 2005;35(4):426-433.

121. Parker EA, Israel BA, Robins TG, et al. Evaluation of Community Action Against Asthma: a community health worker intervention to improve children's asthma-related health by reducing household environmental triggers for asthma. *Health Educ Behav.* Jun 2008;35(3):376-395.

122. Williams SG, Brown CM, Falter KH, et al. Does a multifaceted environmental intervention alter the impact of asthma on inner-city children? *J Natl Med Assoc.* Feb 2006;98(2):249-260.

123. Breysse J, Wendt J, Dixon S, et al. Nurse case management and housing interventions reduce allergen exposures: the Milwaukee randomized controlled trial. *Public Health Rep.* May-Jun 2011;126 Suppl 1:89-99.

124. Largo TW, Borgialli M, Wisinski CL, Wahl RL, Priem WF. Healthy Homes University: a home-based environmental intervention and education program for families with pediatric asthma in Michigan. *Public Health Rep.* May-Jun 2011;126 Suppl 1:14-26.

125. Postma JM, Smalley K, Ybarra V, Kieckhefer G. The feasibility and acceptability of a home-visitation, asthma education program in a rural, Latino/a population. *J Asthma.* Mar 2011;48(2):139-146.

126. Smedje G, Norback D. New ventilation systems at select schools in Sweden--effects on asthma and exposure. *Arch Environ Health.* Jan-Feb 2000;55(1):18-25.

127. Bruzzese JM, Evans D, Kattan M. School-based asthma programs. *J Allergy Clin Immunol.* Aug 2009;124(2):195-200.

128. Bruzzese JM, Unikel L, Gallagher R, Evans D, Colland V. Feasibility and impact of a school-based intervention for families of urban adolescents with asthma: results from a randomized pilot trial. *Fam Process.* Mar 2008;47(1):95-113.

129. Clark NM, Brown R, Joseph CL, Anderson EW, Liu M, Valerio MA. Effects of a comprehensive school-based asthma program on symptoms, parent management, grades, and absenteeism. *Chest.* May 2004;125(5):1674-1679.

130. Gerald LB, Redden D, Wittich AR, et al. Outcomes for a comprehensive school-based asthma management program. *J Sch Health.* Aug 2006;76(6):291-296.

131. Kattan M, Crain EF, Steinbach S, et al. A randomized clinical trial of clinician feedback to improve quality of care for inner-city children with asthma. *Pediatrics.* Jun 2006;117(6):e1095-1103.

132. Shah S, Toelle BG, Sawyer SM, et al. Feasibility study of a communication and education asthma intervention for general practitioners in Australia. *Aust J Prim Health.* 2010;16(1):75-80.

133. Fifield J, McQuillan J, Martin-Peele M, et al. Improving pediatric asthma control among minority children participating in medicaid: providing practice redesign support to deliver a chronic care model. *J Asthma.* Sep 2010;47(7):718-727.

134. Long KA, Ewing LJ, Cohen S, et al. Preliminary evidence for the feasibility of a stress management intervention for 7- to 12-year-olds with asthma. *J Asthma.* Mar 2011;48(2):162-170.

135. McCarney R, Warner J, Iliffe S, van Haselen R, Griffin M, Fisher P. The Hawthorne Effect: a randomised, controlled trial. *BMC Med Res Methodol.* 2007;7:30.

136. Katz LF, Kling JR, Liebman JB. MOVING TO OPPORTUNITY IN BOSTON: EARLY RESULTS OF A RANDOMIZED MOBILITY EXPERIMENT. *Quarterly Journal of Economics.* 2001;116(2):607-654.

137. Illi S, von Mutius E, Lau S, Niggemann B, Gruber C, Wahn U. Perennial allergen sensitisation early in life and chronic asthma in children: a birth cohort study. *Lancet.* Aug 26 2006;368(9537):763-770.

138. Liu AH, Jaramillo R, Sicherer SH, et al. National prevalence and risk factors for food allergy and relationship to asthma: results from the National Health and Nutrition Examination Survey 2005-2006. *J Allergy Clin Immunol.* Oct 2010;126(4):798-806 e713.

139. Limbos MA, Chan LS, Warf C, et al. Effectiveness of interventions to prevent youth violence a systematic review. *Am J Prev Med.* Jul 2007;33(1):65-74.

140. Parker RN, Alcaraz R, Payne PR. Community readiness for change and youth violence prevention: a tale of two cities. *Am J Community Psychol.* Sep 2011;48(1-2):97-105.

141. Freudenberg N, Silver D, Carmona JM, Kass D, Lancaster B, Speers M. Health promotion in the city: a structured review of the literature on interventions to prevent heart disease, substance abuse, violence and HIV infection in US metropolitan areas, 1980-1995. *J Urban Health.* Sep 2000;77(3):443-457.

142. Arbes SJ, Jr., Sever M, Mehta J, et al. Abatement of cockroach allergens (Bla g 1 and Bla g 2) in low-income, urban housing: month 12 continuation results. *J Allergy Clin Immunol.* Jan 2004;113(1):109-114.

143. Sever ML, Arbes SJ, Jr., Gore JC, et al. Cockroach allergen reduction by cockroach control alone in low-income urban homes: a randomized control trial. *J Allergy Clin Immunol.* Oct 2007;120(4):849-855.

144. Wright RJ, Cohen RT, Cohen S. The impact of stress on the development and expression of atopy. *Curr Opin Allergy Clin Immunol.* 2005 Feb 2005;5(1):23-29.