

Environmental Causes of Asthma in Inner City Children

The National Cooperative Inner City Asthma Study

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Introduction

The prevalence of asthma and morbidity from asthma in the United States continued to increase in figures as recent as 1994 (1). These figures show that morbidity and mortality increased disproportionately among African Americans and among children, continuing trends that have been recognized for the past two decades (2–5). Poverty, ethnicity, and residence in the inner city are closely related in the United States, and considerable effort has been directed at dissecting these factors. There seem to be definite racial differences in prevalence that cannot be accounted for by socioeconomic status. From NHANES II data (6), the rate of asthma among children aged 6 mo to 11 yr was 3.0% in whites, 7.2% in African Americans. Although the rate of asthma was related to age, gender, and residence in the inner city, the ethnic differences were significant even when adjusted for these factors. Similarly, in the Six Cities study (7), the unadjusted prevalence in whites 7–14 years was 4.8% and in African Americans 6.7%, and the differences were statistically significant after adjustment for confounding variables. Hispanic children also have a higher prevalence of asthma (4). Morbidity from asthma is also higher in minorities (4); however, poverty seems largely to explain these differences (8). Mortality from asthma is as much as three times higher in minorities (4), and the relation of mortality to African-American and Hispanic ethnicity has been found by some (3) but not all (9) investigators to be explained by poverty. Taken together, these studies suggest that the

three components of ethnicity, poverty, and residence cannot be dissected easily, and should be viewed together when trying to understand risk factors for asthma.

A number of factors have been proposed as responsible for the increased prevalence and severity of asthma among inner-city children. These can be grouped into large categories: access to medical care, patterns of medical care, psychosocial stress, and environmental exposures. In discussing these factors, this review will rely heavily on published data from the National Cooperative Inner-City Asthma Study (NCICAS). This was a multicenter epidemiologic study conducted in eight eastern and midwestern US cities from 1991–1996 to determine the risk factors for asthma severity in 1528 children aged 4–9 yr. The children and their families were recruited from emergency rooms and medical clinics if they had a diagnosis of asthma and if they lived in a neighborhood with a high prevalence of poverty. A clinic visit was conducted within a month of recruitment in which the children and their caretakers underwent extensive interviews, then inscribed spirometry and prick-puncture skin testing to 13 inhalant allergens, and provided a urine sample for cotinine analysis. Home visits were conducted on 653 homes to inspect with a checklist, to collect settled dust samples for analysis of allergen content, and to leave a passive detector of NO₂ content of bedroom air. In the ensuing nine months, families were called to assess continued morbidity. During the last two years of the study, a randomized controlled clinical trial was conducted with 1033 children to test a global intervention that included avoidance of cockroach allergen and environmental tobacco smoke (ETS).

Access to Medical Care

Early in the 1980s, a survey of Baltimore school children reported that nearly 50% of school aged children who had active asthma received their care for asthma only through the emergency room (ER), and that 58% of these children had had at least one ER visit for asthma in the past 6 mo (10). In the NCICAS, acute care was delivered predominantly in the emergency room (11,12) but almost all children reported having a place for routine care, most commonly in a neighborhood health clinic or a university pediatric clinic. Children with less severe asthma were significantly more likely to go to a physician's office or clinic for care of acute attacks and were more likely to have their care in a physician's office. Most (73%) paid for their care through Medicaid. This pattern was the same reported in a nationwide cross-sectional survey, the National Health Interview survey (NHIS), which included comparative data for more affluent families (13). In that survey

poor families were more likely to attend a neighborhood health clinic (15.1 vs 1.6%) or a hospital-based clinic (11.1 vs 2.8%) and were four times more likely to go to an ER for acute asthma care. This type of access to health facilities leads to more fragmented care, creates the need to travel to several sites, and makes telephone advice more difficult, especially because 25–30% of inner city families do not have a telephone in the home (14).

Patterns of Medication Use

Medication recommendations for the treatment of chronic asthma have changed a great deal in the last decade. Currently, guidelines for asthma therapy (15) include daily anti-inflammatory medications such as cromolyn, nedocromil, and inhaled steroids for all patients with moderate to severe asthma, as well as for any patient who requires daily treatment with beta-adrenergic agonist for asthma symptoms. As a result of these recommendations, the use of anti-inflammatory medications has increased sharply, so that by 1993, 22% of asthma medications prescribed by US pediatricians were anti-inflammatory agents (16). One of the strongest pressures to institute these recommendations was the epidemiologic evidence that began to accumulate suggesting that increasing dependence on bronchodilator therapy, especially beta-adrenergic agents, was contributing to the world-wide increase in deaths from asthma (17).

Medications used by children in the inner city are similar to those used by the asthmatic population in general (11,16–19). In NCICAS, 51% of families reported that their child relied only on beta-adrenergic agonists for asthma and that 66% included beta-agonists in treatment (11). These numbers are higher than the 45% found in 1986 in the Michigan Medicaid population, which was older (20), but are similar to the 56% of school children reported from a 1993 survey from Baltimore and Washington who used beta-adrenergic agonists (21). Daily theophylline therapy was reported by 19% of NCICAS school children and by 31% of the children in the Baltimore/Washington survey. Finally, inhaled steroids and cromolyn were reported by 28% of the NCICAS sample and by 10% of the children in the Baltimore/Washington survey. These figures compare to national asthma prescription figures for children in 1993 of 71% beta-agonists; 7% theophylline; and 22% cromolyn, nedocromil, or inhaled steroids (16). These data confirm and expand earlier reports (18,19) of inappropriate asthma medication use among inner city children with asthma. In addition to this pattern of high use of theophylline and low use of anti-inflammatory medications, it is important to note that a substantial proportion of inner city children used beta-adrenergic drugs alone.

This pattern of reliance on beta agonists alone could lead to more unstable asthma (17). Both the NCICAS and the Baltimore/Washington surveys found that many children with asthma in the inner city took no medication for their asthma, despite frequent symptoms, ER visits, and school loss.

Another important behavior found in the Baltimore/Washington survey is that many children in the inner city assumed responsibility for their asthma medications at a relatively young age. The parents of 50% of 9-yr-old children and of 17% of 6-yr-olds reported that their supervised their own medications. It would be important to know to what extent these children assumed responsibility, but this finding is consistent with the other indications of high utilization of symptomatic medications and general under-medication. Self-management increased when the parent worked outside of the home, suggesting that working mothers may have to delegate most responsibility to the a child at an earlier age. Because there is data showing that children and adolescents with diabetes mellitus who are given greater responsibility for their self-management demonstrated poorer metabolic control (22), future studies should examine this behavior in inner city families. At present, we would urge all physicians caring for inner-city children with asthma to ask specifically about responsibilities of the child and advise parents when these seem inappropriate.

Psychosocial Stress

The stress of poverty creates a number of specific issues that could impact on asthma. The NCICAS data provided the most comprehensive examination of these factors and their relationship to asthma severity. The vast majority of caretakers (96%) were women, usually single (54%) and unemployed (49%). In keeping with previous data from young inner-city mothers, 18% of the children were reported to have low birth weight, 25% were in an neonatal intensive care unit at birth, and 10% were on a respirator (11). In describing their own psychological status, caretakers reported high levels of psychological symptoms. Using a standardized questionnaire, the Brief Symptom Inventory (BSI) mean score was 56, and 50% of the caretakers met the test criteria for referral for psychiatric counseling. The children were given a similar screening questionnaire, the Child Behavior Checklist (CBCL), and 35% met the criteria for referral based on their response. Maternal and child symptom scores were closely correlated and both related to asthma morbidity (23). From the CAGE questionnaire, 9.5% were identified as having a potential drinking problem, but this compares to 10.6% in the general population. The families' asthma knowledge was excellent, and they scored an average of 85 on asthma knowledge exams. However,

the use of this information was inconsistent, and when they were asked to respond to hypothetical vignettes, such as a child with acute asthma on a family activity away from home, families were able to generate less than one solution and frequently provided an undesirable response.

Environmental Exposures and Asthma

It has been suggested that urban pollution might contribute to increased asthma morbidity in the inner city. However, ambient air pollution has been declining steadily in US cities (9) at the same time that asthma morbidity and deaths have increased, so other factors must be more strongly associated. Until recently, indoor environmental exposures have not been studied extensively, but available evidence suggests that the indoor environment is more closely associated with the frequency and severity of asthma.

Environmental tobacco smoke (ETS) is the indoor pollutant most closely linked with increased asthma prevalence and morbidity (24–26). Chronic, symptomatic asthma is more common in children exposed to ETS at home, with Relative Risks of up to 2.5 (25). In addition, the severity of asthma symptoms and pulmonary function decrement (26) is related to heavy ETS exposure. Although no direct comparisons between middle-class and inner-city populations are available, a study in an urban ER reported over 50% of children had at least one smoker in their homes, and over 38% had elevated urinary cotinines compatible with heavy exposure to environmental tobacco smoke (24). In general population surveys, smoking exposure is not related to race. As reported in the Six City Study (7), over a pack-a-day consumption was reported by 30% of white mothers compared to 17% of African-American mothers. The same study reported smoking by 2.4% of 14-yr-old white boys, 11.7% of 14-yr-old white girls, 4.1% of 14-yr-old African-American boys, and 6.7% of 14-yr-old African-American girls. These figures represent the total population and did not separate ethnic groups by income, but the report by Ehrlich and colleagues suggests that ETS exposure is high among inner-city asthmatic families (24). In NCICAS, 59% of the families had at least one smoker in the home, with 39% reporting that the primary caretaker smoked. In addition, urinary cotinine were elevated (above 30 ng/g creatinine) in 48% of children. These figures suggest that exposure to environmental tobacco smoke in the home is more common in inner-city homes, but it is not known how important this is as a cause of increased morbidity.

Another indoor pollutant considered in relation to asthma is nitrogen dioxide (NO₂). Nitrogen dioxide is an industrial pollutant that is generated as a by-product of hydrocarbon combustion and is

considered to be an important component of urban smog. It is generated in homes by gas stoves and space heaters but indoor concentrations are rarely elevated to levels that are considered health risks. Indoor NO₂ was measured in NCICAS and was as high as 480 bpb with 24% of families exposed to levels of 40 ppb or greater (11). These excessive levels were thought to relate to gas use by 89% of families and the fact that 24% of kitchens did not have functioning windows. To put this in context, the EPA air standards consider annual average levels of 50 ppb to constitute a risk factor for acute and chronic lung disease, and computer modeling of data from the Six Cities Study demonstrated that levels over 30 ppb would result in annual exposures of greater than 50 ppb (27). Thus, inner-city homes frequently contain levels of an important pollutant in excess of EPA environmental standards, and this could be expected to contribute to asthma morbidity.

Exposure to indoor allergens has recently been reported to be a source of respiratory morbidity. Between 60 and 80% of children and young adults with asthma have one or more positive skin tests to aeroallergen (28,29) and those who do have significantly more severe asthma. In limited studies with inner-city populations, similarly strong associations have been found between sensitization and asthma. Asthmatic patients in urban clinics have been found to have high frequencies of positive skin tests (30–33), but the pattern of specific sensitivities differs from that in the general population, with a higher frequency of sensitivity to cockroach and molds and less frequent sensitivity to cats, dogs, and house dust mites. The question of allergic sensitization and the degree of allergen exposure were among the risk factors considered important to asthma severity in the design of the NCICAS. At baseline, the children were skin-tested using a Multitester® device (34) to 15 allergens (*D. pteronyssinus*, *D. farinae*, *alternaria*, *helminthosporium*, *penicillium*, cat, dog, rat, mouse, German cockroach, American cockroach, oak, maple, grass, and ragweed pollen. At least one positive skin test was seen in 77% of children, and 47% had three or more positive tests. The most common positive skin test was *alternaria* (38%) followed by cockroach (36%), and house dust mite (35%). Allergy to rat (19%) and mouse (15%) was almost as common as allergy to cat (24%) and dog (16%). Most children were sensitive to several allergens (11).

The distinct pattern of skin-test reactivity is mirrored by the pattern of allergens found in inner-city homes. Fungal contamination was found in almost every sample of settled dust from homes in a metropolitan area (35). Recently, an elegant epidemiologic study found that outdoor mold-spore exposure was closely correlated with symptom scores in a group of sensitized asthmatic patients (36). Insects

such as cockroach that infest homes have been implicated in several urban studies. Call (37) and Gelber (38) examined settled dust from inner-city homes and found high concentrations of cockroach allergen. Therefore, it appears that exposure to any environmental allergen, if it is intense and persistent, may lead to sensitization in atopic persons and may then be associated with chronic asthma.

Allergy to cockroach has been described in urban poor populations for many years (30–32). In these studies, race, poverty, and living conditions are heavily interrelated and it is difficult to tell whether exposure and sensitization relates to one factor more than another. The report by Garcia and colleagues (39) that the rural poor in Kentucky had a high sensitization rate suggests that it is not strictly an urban problem. Our own studies with a group of well-characterized children who were participating in a clinical trial suggest that both race and socioeconomic status may be important (40).

In the NCICAS, 653 homes were visited to inspect and collect household dust samples to measure dust mite (Der p 1, Der f 1), cat (Fel d 1), and cockroach (Bla g 1) allergens (41). At these visits, we found the homes to be old and in poor repair, with leaky roofs (12%) and broken windows (13%). Wall-to-wall carpeting was common (41% of TV/living rooms, 32% of bedrooms), but only 38% of homes had functioning vacuum cleaners. Signs of infestation with cockroaches or mice were seen in 66% and 29% of homes, respectively. Bedroom dust allergen analysis is presented in Table 1.

Because others (37,38) had found that children who were both sensitized and exposed to high concentrations of allergens in their homes were more likely to have asthma, this relationship was examined in the NCICAS. Morbidity data was also collected in a questionnaire at baseline. At 3, 6, and 9 mo after their enrollment, a trained interviewer collected the same data using a telephone questionnaire or in an interview with the family if they could not be reached by telephone. Eighty-six percent of families completed all 4 assessments. Follow-up data was incorporated with the baseline questionnaire to give a 12-mo picture of the child's asthma morbidity that detailed the symptoms from asthma, their utilization of physician's offices, ERs, and hospitals for acute symptoms, as well as the effect of these symptoms on daily activities (33).

In Fig. 1, it can be seen that the sensitized and exposed children have greater asthma morbidity in a number of areas (42). For example, the frequency of hospitalization in this group is almost three times higher (0.37 hospitalizations per child/yr) and unscheduled visits are almost twice as frequent (2.56 visits per child/yr). These differences are significant ($p < 0.01$) even when adjusted for the three strongest covariates (gender, CBCL score, family history of asthma). The association

Table 1
Allergen Concentration in Dust From Bedrooms of Children with Asthma
Living in United States Inner Cities^a

	Cockroach	Mite	Cat
Detectable allergen	89%	49%	86%
% above threshold ^b	50%	9.7%	13%
Median concentration	8.2 U/g	0 µg/g	0.1 µg/g
Maximum concentration	1190 U/g	39 µg/g	167 µg/g

^aData based on analysis of settled dust from 476 childrens' bedrooms (42).

^bThreshold for high exposure used for the study: roach, 8 U/g; mite, 2 µg/g; cat, 2 µg/g.

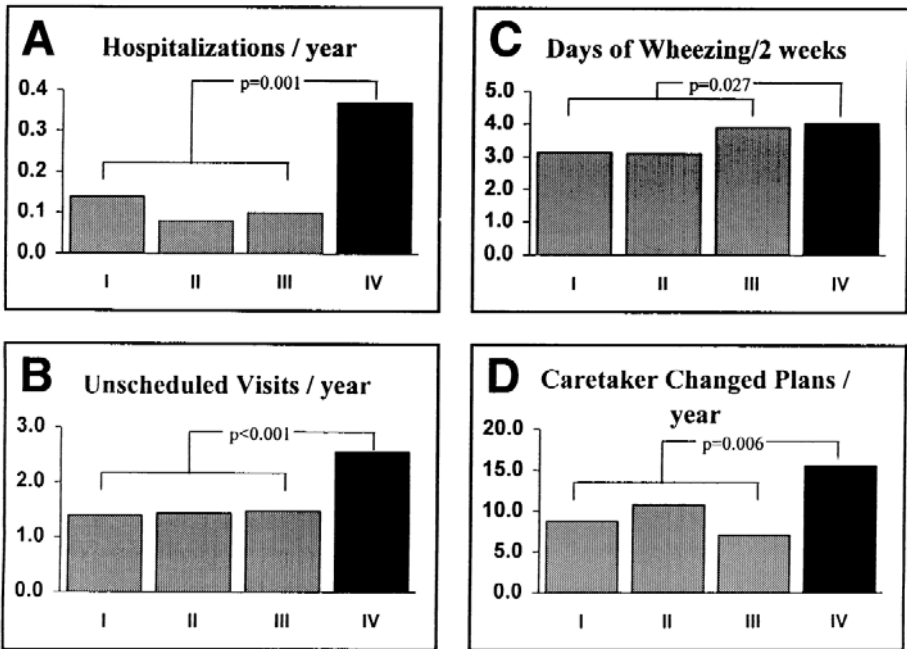


Fig. 1. The association of sensitization and exposure to cockroach, cat, and dust-mite allergens on hospitalization rates for asthma in 476 children enrolled in the NCICAS study (42). Group I had negative skin test and exposure, group II had negative skin test but positive exposure, group III had positive skin test but no exposure; and group IV had both positive skin tests and exposure. Exposure was assessed using bedroom dust samples.

between sensitization and exposure to house dust mite or cat allergen and asthma morbidity was not statistically significant. However, the numbers of children who were both sensitized and exposed to house dust mite or cat was small (15 children) and the power of this study to test the association was inadequate. These data confirm the importance

of IgE-mediated hypersensitivity in chronic asthma. Within inner-city children, who are at greatest risk from asthma in the United States, these data suggest that allergy to cockroach is a specific and important risk factor.

The NCICAS data allowed us to examine the relationship between allergen exposure dose and the risk of sensitization to that allergen. Several previous studies of this relationship had given conflicting results. Chan Yeung (43) failed to find that the concentration of dust mite allergen in individual homes related to the rate of sensitization of children living in the homes. Peat and colleagues (28) studied the rate in several Australian towns with extremely different climates and large differences in dust mite allergen concentrations and showed that the rate of sensitization to house dust mite was much higher in communities with high concentrations of house dust mite. Kuehr studied mite allergen exposure in household dust over 2 yr. The risk of developing a positive skin test to mite increased linearly at concentrations higher than 2 $\mu\text{g/g}$ of mite group 2 allergen (44). In NCICAS, the relationship was only significant for cockroach allergen. The lack of relationship could be explained by the high frequency of household dust samples with undetectable levels of these allergens (45) (Fig. 2). It appears that the risk of sensitization increased at very low exposures and that levels above 4 U/g incur no further risk. The existence of a dose response confirms earlier data from Australian and Germany, but the specifics of the relationship implies that very low levels must be achieved to affect the sensitization risk.

There were no deaths among these 1528 children during the year that they were observed, so there is no information directly bearing on asthma mortality. However, the association that we saw between allergen exposure in sensitized children and asthma morbidity suggests that atopy is likely to be a risk factor for mortality as well. The strongest associations in our data were with hospitalizations and ER visits for asthma, which are consistent with the increased severity of the group, but might also indicate that asthma instability and susceptibility to acute severe attacks is increased. Seasonal allergen exposure has been shown to increase airway hyperresponsiveness (46) in the same way that allergen inhalation challenge increased for several days if a LPR was induced (47). One could speculate that the data from NCICAS indicated that indoor allergen, in this case cockroach, increased hyperresponsiveness and led to increased attacks that were difficult to control at home so that they were more likely to require acute medical care and to have asthma that could not be controlled with their usual medications.

Although exposure and sensitization to cockroach allergen was associated with more severe asthma, several points should be addressed

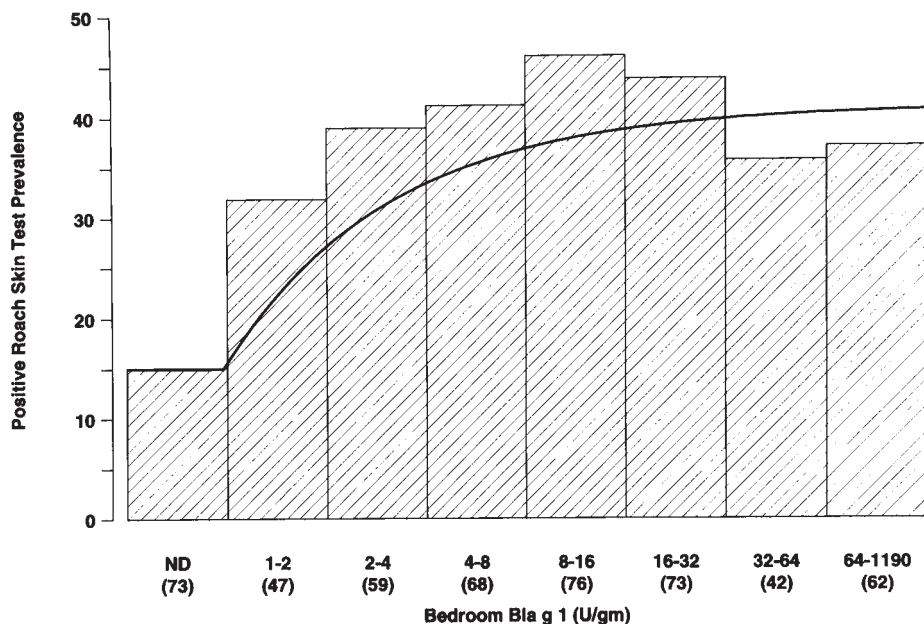


Fig. 2. The relationship between Bla g 1 concentration and the frequency of sensitization (45). Figures in parentheses represent the number of children with bedroom allergen levels in the range indicated, and the height of the bars represents the percent of children with a positive skin test to cockroach extract. The solid line is the summary of the relationship for all children.

in future studies of this risk factor for increased asthma prevalence and severity. Exposure assessment is complex because the children that we studied were sensitive to many allergens and were likely to be exposed to many of these in their home. In neither the NCICAS study, nor earlier studies, was the interaction of multiple sensitivity and exposure examined, but we would expect that it is important, because the odds ratios that we found in the NCICAS study for the single allergen, cockroach, is about the same that Gelber and Call found for a combination of mite, cat, and cockroach. In addition, allergen exposure assessment still needs to be improved. Although the presumed route of exposure is airborne, settled dust allergen concentration is currently used to estimate exposure because it is more feasible and has been associated with sensitization and disease. When airborne measures are feasible, we would expect stronger associations between exposure and disease. Another concern with our current approach is that single measures are compared to morbidity of a disease that is characterized by rapid changes in morbidity and physiology over time. We know that allergen concentrations vary widely, both in a spatial and temporal sense. Repeated samples of settled dust in the same location or in different locations in the same room (48) vary widely. Allergen levels collected in the same

location vary widely over time, whether settled dust (41) or air (49) is sampled. Delfino and colleagues (36) have taken advantage of temporal variations to examine the influence daily allergen exposure on daily symptoms and FEV1. Such studies are likely to expand and clarify the relationship between allergens and asthma.

The finding of a strong association between cockroach allergen exposure and asthma in the inner city has important public health implications. If it can be shown that disease activity can be changed by reducing cockroach allergen exposure, this will provide an important public health weapon to change the current epidemiology of asthma. In order to reduce cockroach allergen, we must understand abatement. Since the sources of cockroach allergens include the GI tract, saliva, feces and body parts, it will be necessary to clean environments after reducing cockroach numbers through pesticides. A number of effective pesticides are now available (diazinon, chlorpyrifos, carbaryl, avermectin) that are capable of reducing populations in single or multi-family housing by over 90% for as long as 3 mo (50–52). Effective procedures to remove the allergen are not as well tested, although vacuum cleaning (53) and application of 3% Tannic Acid (54) have been shown to be effective in experimental settings. Disease effects of abatement have not been tested, and until this is done we are not in a position to recommend changes in public policy to reduce this important risk factor.

Using the available data from Phase 1 of NCICAS, a randomized controlled clinical trial of an intervention was conducted during Phase 2. The intervention was a global one in which an asthma counselor who was a social worker provided education at baseline regarding asthma symptom recognition, medication, and methods for avoiding asthma triggers, then provided support throughout the year-long intervention. The children who had positive skin tests received mattress and pillow coverings and those who were sensitized to cockroach also received professional pest control, cleaning supplies, and further education on cockroach allergen removal.

The intervention was successful in reducing asthma morbidity (55). The homes of 60 children were visited for an inspection, placement of a passive roach trap, and collection of settled dust for allergen measurement. In these 60 homes, neither the cockroach numbers nor the level of cockroach allergen was reduced (*see* Table 2) (56). We concluded from these studies that cockroach allergen will not be easily removed in inner-city homes and will require further study of cockroach ecology and pest control as well as cleaning methods to allow infested housing to be successfully remediated. We also concluded that the effectiveness of the intervention could not be said to be related to home allergen abatement.

Table 2
Cockroach Extermination in the NCICAS Intervention Trial

	Baseline	1 mo	6 mo	12 mo
Bla g 1 Bedroom ^a	8.9	11	8.4	6.1
Bla g 1 Kitchen	69	34	35	92
Bla g 1 TV/living	8.2	12	6.0	7.4
% homes reporting cockroaches	93	80	88	80

^aU/gm settled dust. Geometric mean values (56).

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