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The School Inner-City Asthma Intervention Study: Design, rationale, methods, and lessons learned

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ABSTRACT

Asthma is the most common chronic disease of childhood in the United States, causes significant morbidity, particularly in the inner-city, and accounts for billions of dollars in health care utilization. Home environments are established sources of exposure that exacerbate symptoms and home-based interventions are effective. However, elementary school children spend 7 to 12 h a day in school, primarily in one classroom. From the observational School Inner-City Asthma Study we learned that student classroom-specific exposures are associated with worsening asthma symptoms and decline in lung function. We now embark on a randomized, blinded, sham-controlled school environmental intervention trial, built on our extensively established school/community partnerships, to determine the efficacy of a school-based intervention to improve asthma control. This factorial school/classroom based environmental intervention will plan to enroll 300 students with asthma from multiple classrooms in 40 northeastern inner-city elementary schools. Schools will be randomized to receive either integrated pest management versus control and classrooms within these schools to receive either air purifiers or sham control. The primary outcome is asthma symptoms during the school year. This study is an unprecedented opportunity to test whether a community of children can benefit from school or classroom environmental interventions. If effective, this will have great impact as an efficient, cost-effective intervention for inner city children with asthma and may have broad public policy implications.

Abbreviations: ACT, Asthma Control Test; CADR, Clean Air Delivery Rate; CASI, Composite Asthma Severity Index; CFM, Cubic feet per meter; Db, decibels; DCC, Data Coordinating Center; FDA, Food and Drug Administration; F_ENO, Fractional Exhaled Nitric Oxide; FEF25–75%, Forced expiratory flow between 25 and 75% of vital capacity; FEV_1, Forced expiratory volume in 1 s; FVC, Forced Vital Capacity; GCP, Good Clinical Practice; HEPA, High Efficiency Particulate Air; HRQL, Health related quality of life; HSPH, Harvard T. H. Chan School of Public Health; ICAS, Inner-City Asthma Study; ICAC, Inner-City Asthma Consortium; IgE, Immunoglobulin E; IPM, Integrated Pest Management; IRB, Institutional Review Board; IT, IPM Technician; MAAIT, Mouse Allergen Asthma Intervention Trial; MARIA, Multiplex array for indoor allergens; μg/g, microgram per gram; μm, micrometer; NIH, National Institutes of Health; NIAID, National Institute of Allergy and Infectious Diseases; PEF, Peak expiratory flow; PFT, Pulmonary Function Test; PI, Principal Investigator; PM, Particulate Matter; QALYs, quality-adjusted life years; RA, Research Assistant; SACCC, Statistical and Clinical Coordinating Center; SAE, Serious Adverse Event; SAP, Statistical Analysis Plan; SICAS, School Inner-City Asthma Study- observational study; SICAS-1, School Inner-City Asthma Study-observational study; SICAS-2, School Inner-City Asthma Intervention Study – clinical trial

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1. Introduction

Asthma affects 12–15% of children in urban United States, accounts for over 14 million missed school days per year,[1] and costs billions of dollars in health care utilization despite aggressive measures to identify remediable causes.[2] Elementary school children spend 7 to 12 h a day in school (primarily in one classroom), making school classrooms akin to an occupational exposure for children. The School Inner-City Asthma Study-1 (SICAS-1) (R01 AI 073964, Phipatanakul) was the first observational American study to comprehensively evaluate the role of urban exposures in school, classroom and home environments and asthma morbidity.[3,4] SICAS-1 showed that classroom-specific mouse allergen,[5] mold, and pollutant exposures are associated with asthma morbidity, adjusting for exposure in the home.[6–8] Until SICAS-1, most studies have focused on home exposures to allergenic and pollutant exposures and their associations with asthma morbidity.[9] Home-based trials have demonstrated that targeted interventions (including air filtration) are effective in decreasing asthma morbidity.[10–13] We used established integrated pest management (IPM) measures that have been shown to reduce mouse allergen exposures in homes.[14,15] We then demonstrated that we could effectively decrease classroom-specific toxic exposures during the academic school year by utilizing classroom-suitable High Efficiency Particulate Air (HEPA) air filters specifically adapted to maximize flow while minimizing noise.[16]

In this paper we describe the School Inner-City Asthma intervention Study (SICAS 2), the next logical step to apply successful school/community-based strategies to determine whether a school/classroom intervention to reduce harmful exposures will efficiently and effectively improve asthma morbidity. We use a two-pronged intervention using classroom particle air filter units and school-wide targeted IPM/cleaning to reduce asthma morbidity in urban school children. Herein, we describe our study design, sampling and intervention methods, analytic approach, and anticipated outcomes. In addition, we discuss the importance of our established, successful community relationships over the past decade, which made us uniquely positioned to give back to the community that, after participation in SICAS-1,[17] want this trial.

Our school-based IPM and air filtration trial to remove particles will have particular relevance to long-term public policy and planning for urban U.S. schools with similar indoor environments. In SICAS1, 17% of elementary school children reported nighttime awakenings due to asthma and 15% had asthma-related school absences in the past year. We expect cost-effectiveness where implementation costs are offset by fewer symptom-days and improved quality of life for children, less health care utilization and less loss of work-days (greater economic productivity) for caregivers. If reduction of classroom-specific exposures leads to improved asthma outcomes, then this approach can be implemented as an efficient and cost-effective strategy to benefit communities of children by improving the school environment.

2. Study design and methods

2.1. Description of study design

SICAS-2 is a factorial, randomized, placebo-controlled, parallel group phase II clinical trial designed to assess the efficacy of classroom air filtration and, randomized, controlled, parallel group school (IPM) environmental intervention in improving asthma control in children with asthma. SICAS-2 is a single-Center environmental intervention study. Three hundred children attending any one of the ~40 participating schools in the northeast from September through June in grades K to 8th (generally ages 4–15) will be enrolled into one of the four random intervention groups (75 per group) as outlined in Table 1

Table 1
Arms of the Study.

Groups	N	Assigned intervention
Cohort A - ARM 1	75	School: IPM intervention Classroom: air filter
Cohort B - ARM 2	75	School: IPM intervention Classroom: sham (placebo) air filter
Cohort C - ARM 3	75	School: control Classroom: air filter
Cohort D - ARM 4	75	School: control Classroom: sham (placebo) air filter

2.2. Intervention

2.2.1. Classroom environmental intervention

After randomization, active or sham (placebo) HEPA air filters are placed in the primary home classroom, where elementary students spend the majority of their day. The students and investigators will be blinded to active versus sham. The Air Filtration System (Coway Co., Ltd., Model AP1013A) efficiently captures particles down to < 0.1 μm in size. To achieve maximum effectiveness with an acceptable noise level (52db), custom modification was made to get a dust-free air delivery rate (CADR) of 106 ft[3]/min (CFM). The air filtration system is designed for rooms up to 400 ft,[2] was effective in reducing particles in our Pilot (4 filters/classroom),[16] and was well-received in the classroom/school setting.

2.2.2. School intervention

The Integrated Pest Management (IPM) schools receive an IPM strategy (extermination with rodenticide, traps, and sealing of holes and cracks), air filters, cleaning reservoirs, and education regarding pest control measures. The intervention procedures will be those that were used in the Boston pilot home intervention study,[14] and the Inner-City Asthma Study (ICAS) Study,[11] and the NIAID funded Mouse Allergen Asthma Intervention Trial (MAAIT).[15] The school-specific IPM will focus on surrounding areas that feed into the classroom and harbor infestation by food and water sources (i.e. cafeteria). This is modeled after the home interventions that work by focusing on the child's bedroom, surrounding areas, and the kitchen. The home-based strategies have been proven as effective strategies for reducing pertinent allergen exposure and a low-cost means of improving health outcomes.[10] Our school-based strategies focus on the child's primary classroom, surrounding areas, and the cafeteria. Unlike home intervention strategies, where it is impossible to blind, the School IPM strategies may also be single blinded, because the students attend school during the day, and the IPM will be conducted after hours when the students are not present. Therefore, staff know which school is randomized to IPM but the subjects will be blinded.

2.2.3. Advantages of interventions to be tested

SICAS-2 will be a factorial design with the classroom randomized double-blind, placebo controlled to air filter/purifier and school being randomized in a parallel fashion to an intervention of IPM/Education/Cleaning versus Control School. This allows us to demonstrate the ability of the air filter/purifier in improving classroom air quality and the school-wide effects (classroom/cafeteria, and surrounding supporting areas) of the IPM intervention. Factorial designs have been validated and established[18,19] as an efficient use of resources to determine the effects of two interventions on similar health outcomes within a cohort. The classroom intervention with the parallel school wide intervention allows us to maximize impact and efficiency in one trial.