Study Title: **Evaluation of the Asthma Management Program to Promote Activity for Students in Schools (Asthma-PASS)**
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Evaluation of the Asthma Management Program to Promote Activity for Students in Schools (Asthma-PASS)

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The study is a 5-year study aimed to evaluate a school-based intervention Asthma management program to Promote Activity for Students in Schools (*Asthma-PASS),* developed in collaboration schools and evaluated in a pilot study with 4 Bronx, NY schools and 109 students with asthma and caregivers. The proposed study will be conducted in up to 60 schools with 416 students with asthma; all study procedures and measures (except spirometry to measure basic pulmonary function for children over age 7 years [about 50% of participants]) in this NIH-funded study have been used in our pilot study, and approved by the NYC DOE IRB (study ID #191) and Einstein/Montefiore IRB (IRB# 2012-443). In the proposed study (in comparison to the pilot study), children will only be asked to answer 4 questions from the Childhood Asthma Control Test [if less than 8 years old] and 85 questions [if older than 8 years] compared to 115 questions children were asked in the pilot study; the rest of the survey questions are completed by the caregivers. We will also not be collecting fitness data which we collected in the pilot study. In this protocol, after each section where in-person procedures are proposed, we have included a section with the **COVID-19 Contingency Plan** (requested by the NIH) in the event that schools close or enrolled students will be participating in a fully remote learning model. We are able to carry out all study procedures and intervention remotely if schools close or enrolled students are using the fully remote model of education. In years 1-2 of the study, we will enroll students from 8 schools that are part of Montefiore School Health Program (MSHP) and these students are patients of MSHP clinics. Four MSHP schools will participate in year 1 of the study. Due to the feedback and requests received from the parents of children with asthma during the COVID-19 pandemic in our other studies, we will be providing COVID-19 related-resources, exercise resources that can be done remotely, and answer questions on COVID-19 and asthma during education sessions for all enrolled participants.

Summary:

Asthma is one of the most common chronic childhood illnesses,[1,2] and is the leading cause of school absences.[3,4] In the U.S., asthma disproportionately affects low-income African-American and Hispanic children residing in inner cities such as the Bronx, New York.[5,6] In the Bronx, asthma hospitalization rates are five times higher and death rates from asthma are three times higher than the national average.[7-9] Asthma prevalence in Bronx elementary schools is as high as 25%.[7] Many studies report disparities in health care utilization, asthma morbidity, and access to care in minority children with asthma.[10-14]

Physical activity (PA) is an important component of asthma management in children. PA can reduce school absenteeism, hospitalizations and medication use.[15-19] Exercise training may reduce the perception of breathlessness by strengthening respiratory and skeletal muscles.[20] In addition, habitual PA may lower minute ventilation, thus reducing the likelihood of exercise-induced asthma (EIA).[21] Several studies have reported decreased severity of asthma symptoms and improved disease control and quality of life in children participating in PA programs.[16-19,22] However, three out of five children with asthma limit their PA.[23] In addition, urban minority children with asthma face barriers to PA on multiple levels. In our prior work (NIH-funded

K23HD065742), we identified several barriers to PA in urban minority schoolchildren with asthma. These barriers include: inadequate access to asthma rescue medications in school, suboptimal prescribing of preventive asthma therapy by primary care physicians (PCPs), lack of school PA opportunities, stigma associated with asthma, parent/child fear of an asthma attack with PA, and lack of teacher confidence in assisting students with asthma. We developed a novel Asthma management program to Promote Activity for Students in Schools (*Asthma-PASS)* in collaboration with schools, parents and community stakeholders to address these key barriers.

We pilot tested *Asthma-PASS* with 109 students with asthma from 4 Bronx elementary schools and their parents to demonstrate proof of concept and preliminary evidence of intervention effectiveness (*NYC DOE IRB protocol #191; Einstein IRB 2012-443*). Results from the pilot study demonstrated significantly greater increase in symptom-free days (SFDs) (primary outcome measure) and PA levels. In addition, preliminary mediation analyses suggested vigorous PA and step counts are mediators of SFDs. We now plan to build upon this work and evaluate in a full-scale randomized trial whether the *Asthma-PASS* intervention reduces asthma morbidity among high-risk urban schoolchildren.

We propose a cluster-randomized controlled trial with 416 children ages 4-12 years with persistent or uncontrolled asthma from up to 60 schools in NYC and adjacent neighborhoods (e.g. Yonkers). Recruitment will continue beyond 416 child-parent dyads (up to 500 anticipated) if a drop-out rate and/or loss to follow up at each assessment timepoint is greater than 10%. Schools will be stratified by size and then randomly assigned to either (1) the *Asthma-PASS* intervention (PCP collaboration to ensure optimal guideline-based preventive asthma care and community health workers to facilitate rescue medication availability in school and provide asthma awareness programming and education for children, parents and school personnel to reduce stigma around asthma and PA) or (2) an asthma management (AM) comparison group (PCP and parent notification of child's asthma status and general asthma education). Both groups will participate in an existing district-wide classroom-based daily activity program ('*Move to Improve'*) or have similar school-based activity opportunities for students.

Study Objectives:

This study has the following objectives:

1. ***To assess the effectiveness of Asthma-PASS in reducing asthma morbidity.*** **Hypothesis 1a (primary):** Children in schools randomized to *Asthma-PASS* will experience a greater improvement in the number of SFDs at 3, 6, 9, and 12 months than children in the AM comparison group. **Hypothesis 1b (secondary):** Children in *Asthma-PASS* will have a greater improvement in asthma control (Childhood Asthma Control Test), quality of life, and pulmonary function, and less health care utilization at 3, 6, 9, and 12 months compared to AM comparison group.
2. ***To assess the effectiveness of Asthma-PASS on increasing PA levels.*** **Hypotheses 2a and 2b (major secondary):** a) A greater proportion of children in *Asthma-PASS* will participate in in-class PA, and b) Children in *Asthma-PASS* will have higher overall levels of PA, compared to AM.
3. ***To identify intervention mediators and moderators.*** We will explore if components of self-management (e.g., self-efficacy, adherence) and PA mediate effects on SFDs. These analyses will aid in our understanding of the pathways by which *Asthma-PASS* impacts outcomes. We will also explore if social and contextual factors (e.g., demographics) moderate the effects of *Asthma-PASS* on SFDs.
4. ***To evaluate the process of intervention implementation.*** We will apply the RE-AIM framework to address the intervention's Reach (participation rates), Effectiveness (outcomes), Adoption (acceptability), Implementation (intervention fidelity), and Maintenance (sustainability of intervention by schools).[24]

Background:

Disparities in Pediatric Asthma: Asthma is one of the most common chronic childhood illnesses,[1,2] and is the leading cause of school absences.[3,4] In the U.S., asthma disproportionately affects low-income African-American and Hispanic children residing in inner cities such as the Bronx, New York.[5,6] In the Bronx, asthma hospitalization rates are five times higher and death rates from asthma are three times higher than the national

average.[7-9] Asthma prevalence in Bronx elementary schools is as high as 25%.[7] Many studies report disparities in health care utilization, asthma morbidity, and access to care in minority children with asthma.[10-14]

Multifaceted Interventions Are Necessary to Improve Asthma Outcomes: Research demonstrates that in order to improve asthma outcomes, interventions must include quality medical care[25] in accordance with recommended guidelines[26] and asthma education of both children and parents.[27-29] To address the multiple factors underlying asthma morbidity in schoolchildren, several multifaceted school-based interventions have been described in the literature to show improved asthma knowledge and quality of life, reduction in symptoms and health care utilization, and fewer asthma-related school absences.[30-33] *There is a lack of comprehensive school-based interventions developed in collaboration with the community that reduce asthma morbidity in urban minority schoolchildren with persistent asthma, the targeted population of this proposal.*

Physical Activity is Important in Asthma Management: National authorities endorse physical activity (PA) for all patients with asthma.[34-36] PA can reduce school absenteeism, hospitalizations and medication use.[15-19] However, three out of five children with asthma limit their PA.[23] Different hypotheses (e.g., reduced airway inflammation,[37,38] increased patency of bronchioles[21,38]) have been postulated to explain the protective nature of PA on asthma outcomes. Inactivity as a result of perceived breathlessness can lead to peripheral muscle deconditioning, which in turn, limits exercise capacity.[39] Exercise training may reduce the perception of breathlessness by strengthening respiratory and skeletal muscles.[20] In addition, habitual PA may lower minute ventilation, thus reducing the likelihood of exercise-induced asthma (EIA).[21] Further, inactivity is a major modifiable factor contributing to childhood obesity.[40] Obesity rates in children with asthma are nearly twice that of non-asthmatic children;[41] in our school-based study 58% of children with asthma were overweight/obese.[42] Obese children with asthma have a high degree of disease morbidity (more days with wheezing and ED use).[43]

Several studies have reported decreased severity of asthma symptoms and improved disease control and quality of life in children participating in PA programs.[16-19,22] However, these studies were conducted outside the U.S. with small numbers of participants; did not use an accelerometer, the most accurate and direct measure of PA in children, or validated instruments, such as Childhood Asthma Control Test (cACT),[44,45] to assess control of asthma. *We will use a rigorous cluster-RCT design, objective measures, and validated instruments to evaluate the impact of a novel school-based intervention that optimizes school asthma management and promotes PA, on asthma morbidity and PA levels in U.S. minority schoolchildren.*

Barriers to Participation in Physical Activity Among Urban Minority Children with Asthma: PA levels are low among U.S. youth[46,47] but are even lower in children with asthma due to barriers to participation[48] such as illness beliefs of children (e.g., asthma interferes with exercise)[49-52] and parents (e.g., fear about asthma attacks with PA);[53,54] lack of knowledge of school personnel around asthma management and PA in schools;[55-63] and environmental factors (e.g., lack of staff and facilities to provide physical education (PE)).[64-66] Further, many US children with persistent asthma do not receive effective preventive medications, and thus are limited in their activities due to ongoing symptoms.[67-70] Finally, exercise can increase airway resistance in 70-90% of patients with asthma.[71] Although this can be prevented or reduced by optimal preventive therapy and pre-treatment with a bronchodilator,[71,72] the fear of inducing EIA prevents some children from participating in PA.

We identified barriers to PA in urban minority children ages 7-10 years with asthma at the child/family, school, and health system levels (K23-HD065742, PI Reznik). *Child/Family Level Barriers:* As in our prior study with adolescents,[73] most children reported asthma-related stigma, e.g. feeling embarrassed, shy or concerned about being teased by classmates if they use an asthma pump in front of others or cannot keep up during PA.[74] The most common methods of managing EIA symptoms were sitting out during PE class, drinking water and less often, visiting a school nurse.[74] Common barriers to PA reported by parents were worry about asthma attacks with PA, poor medication adherence, lack of knowledge about EIA therapy, limited PA opportunity at school, and lack of trust in school personnel's ability to manage acute asthma.[53,54] *School Level Barriers:* NYC schools do not meet the New York State Education Department's (NYSED) PE Regulations (at least 120 minutes of activity each week) due to lack of physical space and trained personnel.[75] In fact, Bronx and other New York City (NYC) schools have limited use of playground areas, about 94% of NYC schools are without athletic fields, and 18% of schools do not have a gymnasium.[76] Teachers lack training, knowledge, and confidence in handling asthma.[77] Moreover, we found a lack of written asthma policies in schools with ineffective ways of identifying students with asthma.[9,77] Teachers and nurses usually identified students with asthma through informal conversations with the student or parent or when a student had active symptoms at

school.[78] Further, schools did not facilitate asthma management around exercise and often discouraged PA. Lack of knowledge about the importance of PA in children with asthma and how to manage an asthma attack in schools leads to unnecessary restriction of PA.[48,79] Few parents submitted a physician-completed medication administration form (MAF) to confirm asthma and allow medication administration during school, making school asthma management challenging.[9] Without a MAF, where the PCP specified that the child needed pre-exercise rescue medications administered, children with asthma often 'sat out' and were not allowed to (or were not able to) fully participate in PE or other PA opportunities. *Health System Level Barriers:* In our pilot study, 76% of students had persistent or uncontrolled asthma and 38% lacked appropriate preventive medical therapy (i.e., no controller medication).

In collaboration with stakeholders, we developed a novel comprehensive Asthma management program to Promote Activity for Students in Schools (*Asthma-PASS*), to optimize asthma control and address the identified barriers to PA at child/family, school, and health system levels (***Table 1***). *Asthma-PASS* includes *optimization of asthma control* for safe and full participation in PA through collaboration with Primary Care Providers (PCP) to ensure proper medical treatment as per NHLBI guidelines[26] and MAF completion; a school-wide asthma awareness week to address stigma; asthma education delivered by Community Health Workers (CHW) to children with asthma, caregivers, and school personnel to address fears about asthma and PA and provide education on asthma management to promote PA. CHWs will also ensure MAFs and rescue medication availability in schools. All schools will have a PA opportunity including an in-class activity program, called ***Move-to-Improve (MTI)***), which has been endorsed by the NYC DOE since 2015 as part of a required classroom routine (see **Letters**) to address lack of PA in schools, provide opportunity for students with asthma to engage in PA, and foster PA among *all* students.[80,81] Schools without MTI have other similar school-based activity opportunities/programs for students. *Asthma-PASS builds upon our prior work and overcomes key barriers to PA among high-risk children. Asthma-PASS will enable children to participate in existing PA opportunities and experience improved asthma outcomes by optimizing asthma control, assuring adequate knowledge of asthma, and empowering children to be active.*

Table 1. Identified Barriers to Physical Activity (PA)[a]	Asthma-PASS Components
Child/Family Level	
Asthma stigma	Asthma Awareness Week
Fear of asthma attacks with PA, poor medication adherence, lack of knowledge about EIA therapy	Child/Caregiver Asthma Education; PCP collaboration
Lack of participation in PE and other activity	Facilitate participation in PA
Distrust in school's ability to handle asthma attacks	School Personnel Training; Child/Caregiver Asthma Education
School Level	
Teachers' fear and lack of knowledge on how to handle attack in classroom, during PE and recess	School Personnel Training
No Medication Administration Form (MAF) on file at school	PCP collaboration
Health System Level	
Lack of appropriate medical therapy	PCP collaboration
[a]Qualitative methods used in pilot study to identify barriers to PA. EIA=Exercise-Induced Asthma; PE=Physical Education; PCP=Primary Care Provider	

School-Based Asthma and Physical Activity Programs Are Ideal for Urban Children with Asthma: School-based programs can reach large numbers of children in the settings where they spend most of their day. Several school-based interventions focusing on asthma education and management have improved asthma outcomes.[30-33] School-based programs focusing on increasing PA in healthy children showed improved behavior and activity levels.[82-86] In a prior study of 988 students, we demonstrated feasibility and impact of the in-class activity program on increasing PA levels.[87] *To our knowledge, Asthma-PASS is the first school-based asthma management intervention developed in collaboration with stakeholders with the goal of reducing morbidity and improving PA in urban minority children with asthma.*

Preliminary studies:

1. Experience with Large School-Based Cohort Studies: Dr. Reznik was Co-Investigator on a trial to evaluate the efficacy of an in-class PA intervention, called CHAM JAM (RC1HD063607, PI Ozuah) on increasing PA levels in 10,098 Bronx elementary school students. CHAM JAM promotes PA and reinforces academic learning objectives. We developed CHAM JAM lessons for kindergarten-5th grades; lessons are read by professional actors with contemporary music mixed and recorded in a studio on CD-ROM/mp3. Baseline data showed that less than 1% students (n=916) achieved the recommended minimum number of steps per day.[88] Three months post-CHAM JAM, intervention group students took significantly greater mean number of steps than controls (2848 (SD 1287) vs. 2545 (SD 1153), p=.0036),[87] which is consistent with results of similar programs.[89] *There were no reports of injuries or EIA requiring school nurse visits due to CHAM JAM*

participation. However, during this study we observed many children who would not participate in CHAM JAM activity. Teachers reported that these children claimed to have asthma and would avoid participation in any PA, but there was no documentation on file at the school (i.e. MAF) confirming asthma and no pre-exercise medication listed on a MAF by the child's physician. This observation led to the study (K23HD065742, PI Reznik) to identify barriers to PA in schoolchildren with asthma and subsequent development of the *Asthma-PASS* program to address these barriers. The currently implemented in-class activity program (MTI) is similar to CHAM-JAM but uses paper materials for the teachers to follow specific lessons and activities rather than recordings. ***Importantly, the MTI program is now incorporated into all Bronx schools included in this study.***

2. Experience with School-Based Interventions: *Asthma-PASS* pilot study results. We developed *Asthma-PASS* (K23HD065742, PI Reznik) with stakeholders and tested it in a pilot cluster-RCT. Using a survey, we screened 1270 students (response rate=61%) from 2nd-5th grades in 4 Bronx elementary schools for asthma and identified 74% more students with asthma than the schools did with their methods.[9] Two schools were randomly assigned to receive the intervention and two were usual care (UC). We enrolled 89% (n=109 child-parent dyads, n=60 intervention, n=49 UC) of eligible children (7-11 years of age); 76% had persistent/uncontrolled asthma. In intervention schools: students' PCPs were asked to complete a MAF to confirm asthma and allow for asthma rescue medication administration for exacerbations; children and their parents received an asthma education lesson delivered by trained CHWs and focused on asthma self-management and PA; teachers received an asthma workshop; children participated in classroom-based PA (CHAM JAM) 2-3 times/day; and we held an asthma awareness week. ***One year retention rates were 96% for children (n=58 intervention, n=47 UC) and 91% for parents (n=54 intervention, n=45 UC).***

Table 2. Asthma-PASS intervention effect on PA levels in children with persistent or uncontrolled asthma

	School Hour Data Analysis		Full Day Data Analysis	
	**b_6 (p-value)	**b_{12} (p-value)	**b_6 (p-value)	**b_{12} (p-value)
Moderate PA	1.04 (0.35)	**2.74 (<0.01)**	0.86 (0.73)	3.11 (0.18)
Vigorous PA	**1.59 (0.03)**	**3.03 (<0.001)**	2.24 (0.24)	1.77 (0.34)
Total MVPA	2.63 (0.09)	**5.78 (<0.001)**	3.09 (0.45)	4.88 (0.21)
Step Count (1000)	**568 (<0.01)**	**527 (0.01)**	785 (0.17)	532 (0.18)

PA=physical activity; MVPA=Moderate-Vigorous PA. GEE was used to control for within subject correlation; analysis adjusted for age, gender, BMI, gym, recess, and other activities during school.
** b_6, b_{12}: Group mean difference in change from BL to 6 mo. and 12 mo. respectively.

Findings from this pilot study demonstrated that among children with persistent/uncontrolled asthma (the proposed study population), children in the intervention group had a significantly greater increase in symptom-free days (SFDs)/2 weeks compared to UC (β=1.98, p=0.015), a larger effect than in more intensive and costly asthma interventions.[90,91] Results revealed a significant intervention effect on in-school PA (measured using GT3X+ accelerometers) on minutes of moderate, vigorous, total moderate-vigorous PA (MVPA) and step counts (***Table 2***). There was a trend for students who participated in ≥1 CHAM JAM session to have more SFDs than those who did not (mean difference=0.82 days, p=.063). Preliminary mediation analyses demonstrated that vigorous PA and step counts were mediators of SFDs immediately post-intervention (β=0.24, p=0.003; β=0.001, p<0.001, respectively) and step counts remained a mediator at 12-month follow-up (β=0.001, p=0.014). Full day PA analysis (***Table 2***) showed similar intervention effects to that of the school hour analysis, but did not reach statistical significance due to lack of out of school PA opportunities; thus, enhanced opportunity for in-school PA is critical in assuring children are active. Post-intervention, parents were less likely to believe that exercise is harmful to asthma and less worried about stigma than controls (***Table 3***). Students were less likely to feel that exercise would have negative consequences on asthma and less worried about asthma-related stigma (***Table 3***). Intervention group students had improved adherence scores (measured with a validated Horne's Adherence Scale) on controller medication use post-intervention (3.5 vs. 3.0, p=.007) and at 12-month follow-up (3.3 vs. 2.9, p=.027). ***Our preliminary findings support the effectiveness of Asthma-PASS on improving symptom-free days as well as key secondary outcomes***. ***We have demonstrated our extensive experience with school-based asthma interventions and our ability to successfully recruit and retain high-risk children with asthma***.

Table 3. Pilot Asthma-PASS study preliminary results[a]

	Intervention (n=58)	*Control (n=47)*	*P value*
PARENTS			
Outcome Expectancy – Asthma[b]	.80 (.65; .95)	1.06 (.90;1.22)	.020
Risk Perception – Stigma[b]	1.01 (.74; 1.27)	1.49 (1.21;1.78)	.014
CHILD			
Self-Efficacy – Barriers to PA Participation[c]	2.22 (2.09; 2.34)	2.04 (1.90; 2.18)	.063
Intent to Participate in PA[c]	8.27 (7.84; 8.71)	7.73 (7.25; 8.21)	.098
Outcome Expectancy – Negative Effects of PA[b]	.76 (.61; .91)	1.01 (.84; 1.17)	.035
Risk Perception – Overall Scale[b]	1.92 (1.80; 2.05)	2.14 (2.00; 2.28)	.024
Risk Perception – Stigma[b]	1.55 (1.35; 1.76)	1.90 (1.68; 2.13)	.024

[a]presented as mean (95% CI); PA=physical activity. ANOVA was used to control for baseline scores. [b]lower score = desired; [c]higher score= desired

3. Experience with Community Health Workers (CHWs) to Deliver Asthma Education in the Community: Dr. Reznik is PI of the American Lung Association-funded trial to evaluate the effectiveness of CHWs to deliver a home-based asthma intervention consisting of 6 education sessions to Bronx children aged 2-10 years with persistent asthma and their caregivers.[92] In our *Asthma-PASS* pilot study and our current office-based trial (R01HL133789), we also successfully used CHWs or outreach workers to deliver in-person and telephonic asthma education.

4. Experience with PCP Collaboration: In several of our school-based studies, we contacted PCPs by facsimile, phone or email to ask for authorization of preventive asthma medication administration at school and have been successful >95% of the time.[91,93,94] In our pilot study of *Asthma-PASS,* we sent letters to PCPs via facsimile informing them of the child's persistent/uncontrolled asthma and the guideline-recommended preventive treatment and requesting a MAF for school. We followed up to ensure the MAF was completed and provided to the school. In our pilot, we obtained MAFs for 83% of intervention students compared to 11% that were provided by the UC students. ***In Asthma-PASS, CHWs will follow up with PCPs to ensure provision of guideline-based preventive medications and MAF, as well as rescue medication availability in schools.***

5. Evaluation of Intervention Processes, Physical Activity, Asthma Control and FEV1 Assessments: Several team members have completed process evaluations of community- and school-based interventions,[95] such as RE-AIM[24] and dissemination of asthma self-management programs into urban settings (Reznik, Halterman). Dr. Reznik has developed a protocol for PA assessment and successfully used accelerometers in elementary schoolchildren. Consultant Rowlands is an expert in PA measurement using accelerometers, including data collection, data reduction, processing, and interpretation of findings in relation to health indicators. We collected cACT to assess asthma control in several past[96] and current studies, most recently in a school-based trial with 400 children (R01HL079954) and an ongoing office-based trial with 390 (91% enrollment rate) children enrolled to date (R01HL133789). Our research team has experience measuring lung function (FEV1) in urban children.[96] We successfully obtained FEV1 data in 83% of children ages 7 and above in the school-based study conducted in Rochester City School District Schools by our collaborator from the University of Rochester (R01HL079954).

Implications of the research for New York City schools

The proposed study will evaluate an Asthma-PASS intervention developed in partnership with NYC schools and community stakeholders to best fit it to the needs of NYC students with asthma with the ultimate goal of improving asthma outcomes and physical activity levels in this population.

Physical activity is important in management of asthma in children and has been associated with improved asthma outcomes. However, physical activity levels are low and declining in children, especially in inner-city minority children residing in low-income communities, such as the Bronx, New York and especially now, during the time of COVID-19 pandemic when many children are staying at home and are sedentary. Children with asthma face further barriers to physical activity. Over 50% of Bronx children with asthma are also overweight or obese further adversely affecting their asthma morbidity. Obesity is also a known risk factor for worse outcomes from COVID-19. Promoting both physical activity and healthy weight maintenance may be important aspects of asthma management as well as primary obesity prevention.

Asthma is a chronic disease highly prevalent in the Bronx population, causing severe morbidity and limitation in physical activity. Since asthma is a proposed risk factor for COVID-19 morbidity, asthma control can prevent asthma exacerbations and COVID-19 complications. This project will provide asthma education, support and COVID-19 resources while encouraging physical activity in the population that has been disproportionately affected by both asthma and COVID-19. This study would provide critical new knowledge on the effectiveness of the Asthma-PASS intervention that could help improve asthma outcomes and physical activity during this pandemic or any future epidemics.

Methods:

Study Design: We propose a 2-group cluster-randomized controlled trial of *Asthma-PASS* compared to an AM comparison group. We will enroll 416 dyads of urban children with asthma and one parent from up to 60 NYC schools (primarily, located in the Bronx, NY) and also schools in lower Hudson Valley (if additional schools are needed). To avoid potential contamination, randomization will be at the school level. We will stratify schools based on size prior to randomization to ensure balance of large and small schools among study groups. The study statistician will generate a randomization list for each of the two strata. We will collect follow-up data 4 times (3, 6, 9, and 12 months) during the school year.

Recruitment of study schools: We will recruit up to 60 schools (public, charter, private, catholic) with the following characteristics representative of Bronx and other NYC schools: 1) ~50-80% of students eligible for free/reduced lunch, a marker of poverty; 2) 48%-52% male; 3) 62%-78% Hispanic; 20%-38% African American. In addition to outreaching the schools directly, we will also **i**dentify which schools to recruit and pair to be able to enroll patients of Montefiore. We will use data from Epic to outreach caregivers of students (patients of MSHP or Montefiore, ages 3-11 years) with the diagnosis of asthma based on clinic location and zip code. (Ages 3 and 4 are used to gauge who will be in pre-Kindergarten and Kindergarten the next school year – this age cut off is to be used when we call prior to the beginning of next school year as we plan school enrollment; these children will be in pre-Kindergarten and Kindergarten the following school year when we would approach to enroll them). We will be outreaching telephonically, asking caregivers to confirm their child's school and grade level, which will allow us to identify schools based on proportion of students with asthma (using the EPIC School Outreach Form). We can then outreach school leadership and invite their school to participate. We will also be asking caregivers to confirm if their child has had any asthma symptoms in the last 6 months (if calling 6 months prior to actual enrollment), providing insight regarding possible eligibility for study participation. Once we identify the schools for the study via this method, we will then outreach the patients from these schools via telephone again (regardless of their symptom presence at the initial pre-screening outreach as they may have developed symptoms later on) and screen for eligibility and enroll. If we are contacting the families at the time of enrollment and the schools have been identified as the target schools to enroll, we would conduct the screening for eligibility and proceed with enrollment/consent process.

Subjects and Setting:
416 children aged 4-12 years attending pre-kindergarten-6th grades in about 60 schools (public, charter, private, catholic) and one parent will be screened and recruited into the study at the beginning of each school year over 4 years. Each child will participate for 1 year. The study will include primarily Bronx schools, but other NYC schools with student body characteristics representative of Bronx and NYC public schools in general will be included.

Inclusion Criteria (all criteria must be met)
1) Physician-diagnosed asthma (based on parent report with validation from the child's physician).
2) Intermittent asthma (but with a report of asthma symptoms, such as coughing, wheezing, chest tightness, mucus/phlegm or shortness of breath, in the past 12 months); Mild persistent or more severe asthma based on prescribed controller medication (currently well-controlled) but with a report of asthma symptoms (as specified above) within the past 12 months [well-controlled due to taking controller medications in the past 12 months and without asthma symptoms (as specified above) within the past 12 months will qualify]; or mild persistent or more severe asthma, or asthma that is uncontrolled despite therapy (based on age-specific guidelines):

Mild-Severe Persistent Severity (for children ages *0-4 years* not taking a preventive medication)

Any 1 of the following:

- More than 2 days/week with asthma symptoms (in prior 2-4 weeks)
- 1 or more days per month with nighttime awakenings
- More than 2 days/week use of rescue medications for symptom control (in prior 2-4 weeks)
- "Minor" or more limitation with normal activity (in prior 2-4 weeks)
- 2 or more asthma episodes during the past year that required systemic corticosteroids

Not Well Controlled (for children ages *0-4 years* taking a preventive medication)

Any 1 of the following:

- More than 2 days/week with asthma symptoms (in prior 2-4 weeks)
- More than 1 day per month with nighttime awakenings
- "Some" or more limitation with normal activity (in prior 2-4 weeks)
- More than 2 days/week use of rescue medications for symptom control (in prior 2-4 weeks)
- 2 or more asthma episodes during the past year that required systemic corticosteroids

Mild-Severe Persistent Severity (for children ages *5-11 years* not taking a preventive medication)

Any 1 of the following:

- More than 2 days/week with asthma symptoms (in prior 2-4 weeks)
- More than 2 days per month with nighttime awakenings
- More than 2 days/week use of rescue medications for symptom control (in prior 2-4 weeks)
- "Minor" or more limitation with normal activity (in prior 2-4 weeks)
- 2 or more asthma episodes during the past year that required systemic corticosteroids

Not Well Controlled (for children ages 5-*11 years* taking a preventive medication)

Any 1 of the following:

- More than 2 days/week with asthma symptoms or multiple times a day on ≤ 2 days/week (in prior 2-4 weeks)
- 2 or more days per month with nighttime awakenings
- "Some" or more limitation with normal activity (in prior 2-4 weeks)
- More than 2 days/week use of rescue medications for symptom control (in prior 2-4 weeks)
- 2 or more asthma episodes during the past year that required systemic corticosteroids

Mild-Severe Persistent Severity (for children ages *12 years and older* not taking a preventive medication)

Any 1 of the following:

- More than 2 days/week with asthma symptoms (in prior 2-4 weeks)
- More than 2 days per month with nighttime awakenings
- More than 2 days/week use of rescue medications for symptom control (in prior 2-4 weeks)
- "Minor" or more limitation with normal activity (in prior 2-4 weeks)
- 2 or more asthma episodes during the past year that required systemic corticosteroids

Not Well Controlled (for children ages *12 years and older* taking a preventive medication)

Any 1 of the following:

- More than 2 days/week with asthma symptoms (in prior 2-4 weeks)
- More than 2 days per month with nighttime awakenings
- "Some" or more limitation with normal activity (in prior 2-4 weeks)
- More than 2 days/week use of rescue medications for symptom control (in prior 2-4 weeks)
- 2 or more asthma episodes during the past year that required systemic corticosteroids

3) Attending pre-kindergarten-6th grade in NYC (primarily Bronx) schools and also schools in lower Hudson Valley (if additional schools are needed).
4) Age 4 and 12 years, inclusive.
5) Parent is able to speak and understand either English or Spanish. Participants unable to read will be eligible as all surveys will be administered verbally by research personnel.
6) Consent from the primary caregiver, caregiver permission for child participation as well as assent from the child. If there are eligible siblings, we will randomly select one child to participate.

Exclusion Criteria

1) No access to a phone to conduct follow-up surveys.
2) Family plans to leave the school or city in less than 6 months.
3) The child has other significant medical conditions, such as congenital heart disease, cystic fibrosis, or other chronic lung disease, that could interfere with the assessment of asthma-related measures.
4) Child is unable to participate in routine physical education (PE) classes as per physician-completed sports participation form.
5) Children in foster care or other situations in which consent cannot be obtained from a guardian.
6) Child is a participant in a concurrent asthma intervention study.

Recruitment - Enrollment will occur over 4 consecutive school years with 4-8 schools joining the study each year. Since enrollment will occur over a 2-month time period, we will block enrollment by school pair to assure an equal balance of children in each group for each seasonal time period. We will enroll eligible students/parents in the first 2 months of school with 50 child-parent dyads enrolled in year 1 and 122 child-parent dyads enrolled each school year during Years 2-4. Based on the power calculation, with the total of 416 students from up to 60 schools to be enrolled over 4 years, we will need to enroll 10-16 students per school, that is ~2-4 students per grade per school.

Screening - We will screen students at the beginning of each school year to identify those with persistent asthma. We will send a form home with all students in pre-kindergarten-6th grades to authorize screening and conduct an adapted 6-question asthma screening survey. The asthma screening survey is a brief symptom-focused tool that asks questions about: (a) symptoms with exercise; (b) number of urgent visits in the past 12 months for respiratory symptoms; (c) daytime and nighttime symptoms in the past 4 weeks; (d) rescue medication use in the past 4 weeks; and (e) physician-diagnosed asthma. It is designed to identify students with diagnosed and undiagnosed asthma. If undiagnosed asthma is suspected, we will refer child back to their PCPs for diagnosis and management. Caregivers are asked to provide their contact information on the screening form. The completed screening forms are returned to the teachers in sealed envelopes and collected by the research staff. We will contact caregivers by phone to describe the study, confirm eligibility and schedule an in-person meeting to obtain signed informed consent and child assent. We will also perform screening at school functions, such as “Meet the Teacher Nights,” parent-teacher conferences or health fairs. Research personnel will be available at dismissal time at school to discuss the study with interested parents and children. Flyers advertising the study will be posted around schools.

COVID-19 Contingency Plan:

While NYC public schools are currently open and about 50% of students are attending schools with a hybrid (in-person and remote/online) learning model, below section outlines a fully virtual plan for screening in the event the schools are closed and/or research staff would not be able to attend schools for any study-related activities given COVID-19 precautions.

1. In years 1 and 2 of the study, we will enroll students from schools within the Montefiore School Health Program (MSHP). Letters from the MSHP will be sent to registered students (patients of MSHP) with asthma to describe the study and that study personnel will make phone call attempts unless the family elects to opt out by calling the number listed on the letter. If the caregiver does not call to opt out, the study team will then follow-up with a phone call to the patient/caregiver to provide additional information about the study and conduct eligibility screen/consent process. We will also identify students (patients of MSHP or Montefiore) who had been screened for asthma severity/control via Epic EHR and outreach as described above (mailing letters).
2. For schools without the Montefiore School Health Program (MSHP), which we plan to enroll in subsequent years of the study, the NYC DOE collaborators will mail letters to students with asthma in study schools describing the study and instructing caregivers to call the research team if they are interested in participation.

3. For schools without the Montefiore School Health Program (MSHP) and outside the NYC DOE purview (e.g. charter, catholic), we will collaborate with school personnel and their administration to identify students with asthma. One of the methods will be for school personnel to send letters to students with asthma in their school describing the study and instructing caregivers to call the research team if they are or they are not interested in participation. If the caregiver does not call to opt out, the study team will then follow-up with a phone call to the patient/caregiver to provide additional information about the study and conduct eligibility screen/consent process.
4. School staff, school nurses or clinic staff at any school may refer students with asthma to the study team by sending a letter home with the child or emailing/mailing letter home (for remote students) with the brief study description as described above for the family to contact the research team. School staff or school nurse/clinic staff at any school may also refer students with asthma by first obtaining a verbal approval from the parents (e.g. if speaking with them on the phone about child's asthma or by calling them) to share their contact information with the research team who will then contact the parent to provide further details about the study, and if interested in participation, screen child for study eligibility.
5. At any school, we will also use the 6-question screening for asthma/authorization to screen as described above to send home for children who attend school in person or electronically (e.g. REDCap or another secure platform) for those who are remote learners.
6. We will identify children with asthma who are (1) a MSHP or Montefiore patient (using data from Epic) and (2) attending a study school (using the school screening survey as described above), by calling them and screening for eligibility/enrolling into the study as described above (under Recruitment of Study Schools). We will also review their medical record to identify next upcoming appointment (if unable to reach on the phone) and meet them in clinic to complete screening and proceed with enrollment. Research staff will also be reviewing Montefiore outpatient clinic schedules daily, calling scheduled patients (ages 5-11 with asthma) using the EPIC School Outreach Form to confirm study school attendance and complete eligibility screening and enroll on the phone. If eligible, research staff will ask families to come to their appointment with their physician 30-60 minutes earlier where the caregiver/child will be informed about the study and undergo the informed consent process, completing baseline survey after seeing their physician.
7. Another possibility for identifying participants is via lists from Montefiore CMO. Caregivers of children will be contacted by letters mailed from CMO that explain the research project and establish passive consent to be contacted via phone by research staff about possible participation in the study. The letters will be in both English and Spanish and will provide the recipients with contact information–toll-free telephone number–to use if they wish/do not wish to be called about the study. If the caregiver does not call to opt out, the study team will then follow-up with a phone call to the patient/caregiver to provide additional information about the study and conduct eligibility screening/informed consent process. Any potential participants who call to request not to be contacted will be removed from the recruitment pool, and those who contact the team with interest in the study will be screened for eligibility.

Informed Consent and Baseline Assessment: We will schedule a visit at home, school or another location in the community (e.g. library) to obtain parent informed consent and child assent. Informed consent will be obtained by bilingual (English-Spanish) research staff certified in human subjects research. Baseline measures include an assessment of asthma symptoms, medications and standard family and health history variables and measures. An asthma symptom diary, developed using the school calendar, will be given to the caregiver to track asthma symptoms and school absences. All surveys and recruitment materials will be available in English and Spanish and questions will be read aloud. Informed consent/assent, HIPAA authorization, and a release of medical information will be obtained.

COVID-19 Contingency Plan:

The RAs will use teleconferencing via Zoom or another HIPAA certified/compliant platform, approved for research use by our institution and freely available to Einstein/Montefiore faculty, to remotely obtain consent and child assent.

We believe this is a minimal risk study. During the COVID-19 pandemic, the research staff may not be able to meet with child/caregiver in-person to obtain written consent/assent and the caregiver may not have a smartphone/computer or able to go outside to mail the signed consent forms back. For any subject being consented via phone or video platform, we will follow these procedures: 1) Send the IRB approved informed consent form to the prospective research subject for review, 2) Arrange for a conversation between the research participant and an authorized member of the research team to allow for full discussion of the informed consent form, 3) The research team member will allow for any questions the participant may have to be asked and answered, and 4) We will obtain verbal consent/assent via phone or video platform and the consent process will be documented for each individual subject in their study file.

Baseline surveys will be done via telephone.

All study schools currently participate in the daily required school-wide in-class activity program, called *Move-to-Improve (MTI)*, as part of the NYC DOE initiative to promote PA and help adhere to NY State (NYS) requirement of 120 minutes of PA per week. MTI are 10 minute modules that provide in-class short-burst, education-focused PA that are designed to supplement the existing PE instruction and enhance academic lessons. MTI activities blend academics and physical activity into educational lessons that integrate NYS common core standards curriculum concepts taught in class (e.g., mathematics). Study schools have classroom teachers trained in delivering MTI by the NYC DOE and have been using MTI as part of the classroom daily routine. Teachers use MTI on average 2x/day and all students have the opportunity to participate. The activities are similar to activities during regular PE classes in schools. Teachers have reported that children with asthma do not fully participate in MTI (e.g., sit out). If a child with asthma develops asthma exacerbation while participating in MTI, she/he will be referred to a school nurse as per usual school procedures. All schools in NYC are required to have a nurse on premises during school hours if a student has a medical need (i.e., asthma). In a circumstance when a nurse is out sick, a substitute provides services for that day. Given COVID-19 and majority of students being remote, teachers may use other activity breaks (other than MTI that is led by teachers in the class when all students attend school in-person) during the school day (e.g. GoNoodle, brain breaks).

COVID-19 Contingency Plan:

We are collaborating with the NYC DOE's Office of School Wellness who is overseeing the MTI program at the schools. The below are options for delivery of the physical activity:

1. Teachers in the classrooms with enrolled students will deliver MTI either in-person (for students in hybrid learning model) or remotely.
2. Teachers may choose to use CHAM JAM (if available at their school), a program based on MTI that also promotes PA and reinforces academic learning objectives, instead of MTI during school
3. Alternatively, if teachers will not be able to deliver MTI or CHAM JAM in-person or remotely, research staff will be able to deliver CHAM JAM. Research team can deliver this program remotely via Zoom or another approved audio-video platform 1-2 times a day similar to frequency of MTI delivery. CHAM JAM was evaluated by the study team in 23 schools with over 10,000 students without any incidences of injury or students developing asthma symptoms requiring school nurse or physician visits due to participation. CHAM JAM has lessons for kindergarten-5th grades, read by professional actors with contemporary music mixed and recorded in a studio and available as CD-ROM/mp3. MTI is similar to CHAM-JAM but uses paper materials for the teachers to follow specific lessons and activities rather than recorded lessons.

Asthma-PASS intervention

We will *collaborate with the student's PCP* using established procedures from our prior school-based studies to optimize the child's asthma medications as per NHLBI guidelines,[26] improve adherence, and prevent limitation in PA. We will contact PCPs by sending a letter via facsimile, and/or email to ensure appropriate medications are prescribed or adjusted and rescue medications are available at school. In the letter, we will outline the child's asthma symptoms and the guideline-recommended preventive treatment, and will request a Medication Administration Form (MAF) for school. Community Health Workers (CHWs) will follow up with PCPs by telephone as needed to provide reminders about prescriptions for controller medications and to ensure a MAF is provided to schools to allow rescue medication administration by nurses. CHWs will work with local

pharmacies when possible to have prescribed medications delivered to schools and homes. For students without a PCP, we will refer families to one of Montefiore Medical Center's 20 practices that are situated throughout the Bronx. For students without medical insurance or who are unable to go to a Montefiore clinic, the NYC DOE physicians who routinely attend at NYC schools will provide medical care and prescribe appropriate medications. *Child/caregiver education:* We will provide in-school *child asthma education* sessions delivered by trained, bilingual (English-Spanish) CHWs using an *established* manualized protocol from our past and current studies designed to improve knowledge and self-efficacy. Each child will receive two 1-on-1, 20-minute developmentally appropriate educational sessions at school 3-4 weeks apart. *Caregivers* will be called after each child session to highlight key points reviewed with the child and answer questions. We will collect multiple phone numbers and contact information from other family members/friends in case the caregiver's phone number changes. Both sessions will focus on ways to improve self-efficacy to manage asthma and promote PA. CHWs will address child and caregiver-level barriers to PA such as fears, attitudes and beliefs about asthma and exercise, importance of PA, lack of knowledge about EIA therapy, and importance of medication adherence to control symptoms and enable PA. In our prior work, we developed and delivered via trained CHWs/outreach workers 1 to 6 asthma education sessions per family, in person and over the phone. CHWs will encourage children to participate in PA opportunities in/out of school, including PE, recess and the MTI activity program; review self-management skills; and discuss asthma triggers, proper MDI-spacer technique, and improving communication between child, caregiver, school and PCP. CHWs will also empower and assist families with scheduling visits to the child's PCP, link to care if needed, troubleshoot medication-related issues, and refer to community resources for smoking cessation and pest control. If a child with asthma is unable to participate in MTI, we will ask teachers to notify CHWs to address potential barriers (e.g., ensure controller medication has been prescribed by PCP, MAF is on file with school, and rescue medication is available). We will offer a school-wide *asthma awareness week* - to bring asthma awareness to the school community and address the stigma that students with asthma report.[74] Some activities include asthma and PA slogans and poems displayed throughout the school; student morning announcements on facts about asthma and PA (e.g., famous athletes with asthma); competitions on the best decorated classroom door with student drawings about asthma and PA; and a role play about what to do if someone has an attack. All students in intervention schools will participate in asthma awareness week. *Training school personnel:* CHWs will provide a 45-minute workshop on "Asthma Management and PA in School" based on NHLBI guidelines[26] to all school personnel (e.g., classroom, PE teachers, and recess/lunch aides). It includes a didactic session on overcoming barriers to PA that students with asthma face in school, ways to encourage student PA participation, correct interpretation of symptoms and how to handle an attack in school, promoting communication with the school nurse and caregivers, and a question and answer session. This will address school personnel's lack of knowledge and anxiety around asthma and PA. CHWs will visit schools weekly during the initial optimization phase, monthly (with additional visits if needed) after optimization is accomplished, and then every 2-3 months for ongoing support to address barriers to PA that students or school staff report, and troubleshoot any issues as needed throughout the school year. We will collect data on frequency and time spent on intermittent CHW interactions and troubleshooting encounters with the child/caregiver and school personnel that will help with calculating the cost of intervention implementation.

COVID-19 Contingency Plan:

All Asthma-PASS intervention components described above can be done remotely in case schools are closed or research staff is not allowed to visit schools. CHW can deliver education sessions with child/caregiver on the phone or use Zoom platform to show visuals (e.g. lung/airway model) or demonstrate MDI-spacer technique during education sessions; follow up with the child's PCP to assure optimal asthma management has originally be proposed to be done remotely (by contacting PCPs via email, telephone or facsimile). We will work with the individual intervention schools to plan asthma awareness week activities and school personnel workshop via a webinar using Zoom (e.g. during our pilot study, we were able to do the workshop during teacher Professional Day or during prep/non-teaching time). If CHW will not be able to visit schools, they will schedule Zoom calls with school personnel to provide support and answer any questions that may arise at the same frequency as listed in the original protocol (weekly during the initial optimization phase, monthly (with additional visits if needed) after optimization is accomplished, and then every 2-3 months). CHWs will support families of enrolled intervention group children with uncontrolled asthma (identified via follow-up surveys and also when speaking with caregivers or teachers if child has frequent symptoms) by regular follow-ups via phone, text or Zoom

(monthly check-ins and more often if needed until asthma control is achieved), providing CHW telephone number for caregivers for easy access, connecting them with the PCP and providing support as described above. CHW will ensure that PCPs are aware that children have uncontrolled asthma (by contacting PCPs on the phone), are prescribed controller medications and are able to obtain medications from the pharmacy.

Community Advisory Board (CAB) and Collaborative Board: A CAB with 8 stakeholders (parents of children with asthma, classroom and PE teachers, parent-teacher coordinators, and school leaders) was established for the NIH K23 pilot study. The CAB was instrumental in developing and enhancing intervention components, providing input about implementation, and improving recruitment and retention strategies. We will continue to involve the CAB and meet quarterly via phone (or videoconferencing) or more frequently as needed, with a focus on ultimate sustainability and dissemination. In our pilot study, the parent-teacher association (PTA) and parent volunteers also played a critical role in recruitment and retention of participants by distributing study flyers and spreading the word about the study to the school community. We will engage the PTA in the proposed study to assist with participant recruitment and retention. We have also established a three-member **Collaborative Board** consisting of experts in community-based research (Dr. Bauman), implementation science (Dr. Rinke), and leadership within the New York City Department of Health and Department of Education (Dr. Platt) to provide advice and support during *Asthma-PASS* implementation. The Board members will meet via phone (or videoconferencing) 1-2 times a year and more often if needed to discuss any challenges in implementation of *Asthma-PASS* and offer advice.

Asthma Management (AM) Comparison Condition: We will notify PCPs and caregivers that children in the AM group have persistent/uncontrolled asthma that warrants use of guideline-based preventive medications. We will also provide in-school general asthma education sessions delivered by CHWs (different from the CHWs who will provide education in the *Asthma-PASS* group) using an established protocol, in a similar structure and time-schedule to the *Asthma-PASS* intervention to match the time and attention of the Asthma-PASS group (each child will receive two 1-on-1 developmentally appropriate educational sessions). Sessions will cover: 1) asthma basics, symptoms and triggers; and 2) medications and correct administration technique. As in *Asthma-PASS,* caregivers will be called after each session to review key points from the child's asthma education sessions. AM group is *not* specifically designed to promote PA; CHWs will *not* work with AM group families to empower them and address barriers to child's PA participation (e.g., ensuring medications have been prescribed by PCP, MAF is on file with school, and rescue medication is available); the other components of *Asthma-PASS* such as asthma awareness week and training of school personnel will *not* be provided.

We will offer the workshop for school personnel and asthma awareness week resources to Asthma Management Comparison schools after the final, 12-month assessment is completed for students enrolled in the paired Asthma-PASS intervention schools.

COVID-19 Contingency Plan:
We will use the same procedures to carry out education sessions for the Asthma Management Comparison group as described above for the Asthma-PASS group.

Additional Resources Related to COVID-19:
During all contacts with families in both groups we will offer a list of community resources and supportive services related to COVID-19 (e.g. COVID testing sites, locations of food pantries, mental health community referrals) and answer questions related to asthma and COVID-19 during education sessions.

Training and Treatment Fidelity: CHWs will be trained (4 weeks) by the PI (Reznik) and Co-I (Feldman) using a previously developed manualized protocol based on evidence-based guidelines on asthma self-management skills, proper inhaler technique, triggers, medication use, goal setting and problem solving as related to asthma and PA. We will finalize this training protocol during the R61 phase. After each session, CHWs will fill out a form checking off the components delivered and session duration. We will use the same fidelity plan to ensure that CHW-delivered education to *Asthma-PASS* and AM comparison group is delivered as planned. All CHW education sessions (for child and caregiver) will be shadowed by Sr. Project Coordinator to check that each element is covered in the session. Initially, for the first 1-2 months, PI and Co-I will review all Sr. Project Coordinator observation notes from shadowed sessions and will complete fidelity rating checklists

to ensure sessions are delivered as intended. Once assured that sessions are delivered as planned, 30% of the sessions will be shadowed by Sr. Project Coordinator and observation notes reviewed by the PI and Co-I. These checklists, in conjunction with checks done by Sr. Project Coordinator, will be used to measure education "dose" (#minutes and #components delivered) and treatment exposure. Drs. Reznik/Feldman will oversee CHWs with bi-weekly meetings. As in our prior work, to avoid differential attrition we will assure sessions are interactive and provide flexible scheduling and reminders. Research staff will visit each classroom (in both *Asthma-PASS* and AM schools) at least every other month during the study period to ensure MTI sessions are occurring routinely, as expected, and to assess student/teacher engagement. Research staff will ask teachers in both groups during the one week of PA data collection at baseline and each follow-up assessment timepoint to record if any children did not participate in MTI using a log developed and used in our pilot. Research staff will also visit classrooms daily during PA data collection weeks to obtain this information from the teachers if they were not able to log the data.

Outcomes Assessment and Participant Follow-up Procedure: Assessments will be done in person with both parents and children at baseline and in-person with children while they are still attending schools, at 3, 6, and 9mo (end of school year). We will use structured telephone interviews with parents at 3, 6, 9, and 12mo. Child survey consists of 4 questions from the Childhood Asthma Control Test; all other survey measures will be collected from parents. Follow-up assessments will be conducted by interviewers blinded to the treatment allocation. Research staff will read survey questions to both caregivers and children.

Table 4. Outcomes	Measurement Strategy	Time of Administration
Clinical Outcomes		
Symptom Severity	Caregiver report, NHLBI guideline-based items ***(SFDs, 1° outcome measure)***	Baseline, each follow-up
	Childhood Asthma Control Test (cACT)	Baseline, 3mo, 6mo, 9mo*
Lung Function	Objective measurement (FEV1)	Baseline, 9mo
Health Care Utilization	Caregiver interview	Baseline, each follow-up
Functional Outcomes		
School Absenteeism	Caregiver interview School record review	Baseline, each follow-up Conclusion of school year
School Nurse Visits	Caregiver report, Automated Student Health Record (ASHR) data from NYC DOH/NYC DOE	Baseline, each follow-up Conclusion of school year
Quality of Life	Juniper's Pediatric Asthma Caregiver Quality of Life Questionnaire (PACQLQ)	Baseline, each follow up
Potential Mediators		
Physical Activity	Accelerometers ***(2° outcome measure)***	Baseline, 3mo, 6mo, 9mo
Adherence	Home Adherence Scale	Baseline, each follow-up
Caregiver Knowledge, Beliefs, PCP Relationship	Asthma Illness Representation Scale (AIRS)	Baseline, each follow-up
Asthma and Exercise Self-Efficacy & Outcome Expectancy	Scales developed during pilot study Exercise Self-Efficacy Scale for Children	Baseline, each follow-up - (parent) Baseline, 3mo, 6mo, 9mo*- (child)
Asthma Self-Management	Asthma Self-Management Questionnaire	Baseline, each follow-up
Independent Variables		
Demographics	Caregiver report	Baseline
Body Mass Index	NHLBI Growth and Health Protocol	Baseline, 9mo
Neighborhood Environment; Second-Hand Smoke	Neighborhood Social Cohesion Scale Caregiver report	Baseline, 9mo Baseline, 9mo
Process Evaluation		
RE-AIM Measures	RE-AIM Dimensions	At end of each study year

SFDs, Symptom-Free Days. Each follow-up includes assessments at 3mo, 6mo, 9mo and 12 mo. 3mo data will be collected immediately after intervention; 6mo will be mid-study; 9mo will be at the end of school year; and 12mo final follow-up data will be collected in early September to observe any sustained intervention effects. *Measures obtained directly from children will be assessed at baseline, 3, 6, and 9mo in order to capture children while they are still attending schools.

Measures. ***The primary outcome measure*** is the change in number of symptom-free days (SFDs). Caregivers will report the number of days their child experienced *no* symptoms of asthma (defined as 24 hours with no coughing, wheezing, chest tightness, or shortness of breath) in the past 2 weeks. They will be referred to their symptom diaries to assist with recall. We will collect the primary outcome data at 3, 6, 9, and 12 months post-baseline and we will consider our trial successful *only* if the intervention demonstrates a significantly greater improvement over time on SFDs at any of the 4 post-baseline assessments. We will attempt to schedule follow-up interviews as close to the target date as possible but allow for participants to complete the interview as much as 6 weeks prior to and 6 weeks after that date

Other asthma measures will be assessed at each follow-up (unless otherwise specified). We will assess asthma control with the validated Childhood Asthma Control Test (cACT) for ages 4-11 and ACT for children 12 years and older, both surveys available in English and Spanish.[44] Caregivers will be asked about the child's asthma medications, number of "steroid bursts" for asthma and urgent (acute clinic, ED visits, and hospitalizations) and non-urgent (primary/specialist care) visits.

Functional Outcomes: We will measure self-reported caregiver quality of life using the validated Pediatric Asthma Caregiver's Quality of Life Questionnaire (Juniper's PACQLQ)[97] available in English and Spanish. Data on school absenteeism and on nurse visits due to asthma will be measured by caregiver report (at each follow-up) and school records (NYC DOE's Automated Student Health Record database (ASHR)) at the end of school year.

Potential Moderators/Social-Contextual factors: We will collect the caregiver-reported measures of demographic, personal, and community factors known to be associated with asthma morbidity in high-risk children or influence response to interventions. These include demographics (age,[98,99] race/ethnicity,[100,101] gender,[102] BMI%,[103] insurance,[6,98] second-hand smoke exposure,[104,105] and caregiver education[28,98]). For school and community variables, we will use the validated Neighborhood Social Cohesion Scale,[106] school size, and % free/reduced-price lunch.

Potential Mediators: To explore potential mediators, we will measure PA with accelerometers.[107] At each follow-up, we will measure constructs of self-management: parent-reported preventive medication adherence

(Horne Adherence Scale[108]) and parent asthma knowledge, beliefs, and PCP relationship with the Asthma Illness Representation Scale.[109] We will measure exercise self-efficacy of caregivers and older children (≥ 8 years). The Exercise Self-Efficacy Scale for Children[110] is validated for children ages ≥ 8 years, and will assess how sure children are that they can do PA in a variety of situations (e.g., inclement weather). We will measure caregiver and child (≥ 8 years) asthma and exercise self-efficacy and outcome expectancy with scales developed during the pilot study (Cronbach's α .79 and .76, respectively). We will also assess caregiver self-management behavior with Asthma Self-Management Questionnaire.[111]

COVID-19 Contingency Plan:
In the event that we are not able to obtain baseline assessments in-person or meet children in school due to the COVID-19 restrictions, we will collect survey data at baseline and all follow-up assessments for both children and caregivers by phone. We will use office line or Google phone if research staff would need to use their personal phone in case of telecommuting or use an audio-video telehealth platform approved to be used by the institution (e.g., Zoom) (e.g. to show cACT pictures to children who need to use picture-specific answers for this scale). We will also mail the cACT picture scale to participant's home as part of the recruitment packet (e.g. if the participant does not have access to the smart phone or iPad to be able to use the telehealth platform, we will refer them to the cACT scale included in the recruitment packet). We will continue to collect school absenteeism data over the phone from caregivers (and also obtain these data from the schools/NYCDOHMH/NYC DOE) as children on a hybrid learning model and fully remote model may still be absent from the school activities due to asthma; we will verify with the caregiver which learning model the child participates in at each follow-up.

Pulmonary Function Tests (PFTs): We will use EasyOne® Plus portable spirometer, which meets ATS standards for FEV_1, FEV_1 % predicted, PEF, and FVC, at baseline and 9-month assessments during in-person assessments by the research staff at participant's home/school. We previously used this device successfully in 83% of children over age 7 years in another school-based study. Some of the younger children may have difficulty performing spirometry adequately; we will only include data that meet standard quality criteria. PI will train and supervise staff to perform 20 valid PFTs and then review test results thereafter.

COVID-19 Contingency Plan:

- The above originally proposed plan for collecting PFTs will not be permitted with the current COVID-19 restrictions.
- We will attempt to obtain FEV1, PEF, and FVC at baseline and 9 months for participants older than 7 years (estimate 50% of overall study sample) if funding permits and approved by the IRB by:
    - Mailing an individual digital MicroLife Peak Flow Meter (PFM)[112] (FDA approved and meets American Thoracic Society accuracy standards) or another FDA approved digital PFM with FEV1 capacity to each subject's home for their personal use during the study.
    - Using Zoom platform we will demonstrate participants how to use the device and ask them to read the result of the assessment as displayed on the device back to us at baseline and 9 months (both assessments will be done by participants at their home and results reported to the study team via Zoom).
- The peak flow meter is routinely prescribed to patients (especially those with uncontrolled asthma) by the PCPs and asthma specialists as an objective measure of lung function and it is an important tool used in asthma management to help monitor one's asthma.

Physical Activity (PA) (key secondary outcome measure): We will measure PA (minutes in sedentary behavior, light PA, moderate-vigorous PA, and step count)[113] over 7 consecutive days at baseline, 3, 6 and 9 months using the ActiGraph GT3X+ activity monitor (Pensacola, Florida), a small, tri-axial micro-electro-mechanical system (MEMS) based accelerometer (4.6 cm x 3.3 cm x 1.9 cm; 19 gm). We used this device to collect physical activity measure during our pilot study with 4 Bronx, NY schools. Three-month data will be immediately post-intervention. Six-month data will be used to demonstrate if the intervention has provided sufficient stimulus to increase PA. Nine-month data are collected right before the end of school year. Children in both intervention and AM groups will wear the monitor on their waist, secured using an elastic belt.[114]

ActiGraph accelerometers have been extensively validated and used for assessment of frequency, intensity and duration of PA in children.[115,116] Raw tri-axial data will be sampled at a rate of 30 Hz for 7 consecutive days.[117] Data will be processed using ActiLife6 software through a digitally matched filter and reintegrated up to a 5-second epochs and screened for wear time using methods reported by Troiano.[46] Daily and hourly summary accelerometer estimates will be computed for all participants with at least 4 valid days of ≥10 hours of waking wear time. ***In our pilot study with 4 schools, 99% of participants had valid data.*** We will evaluate activity during school hours and after school. The primary estimate, total accelerometer counts, will be calculated using summed counts detected over wear periods, while the secondary estimates, time (i.e., minutes) spent in different intensity levels will be derived using standardized threshold values.[118] We will collect information regarding scheduled and unscheduled physical activities (PE class, recess, field trips, MTI in-class physical activities, etc.) each day during data collection time points. This information (e.g., PE class schedule, field trips) will be collected by research staff from official class schedules available from each school's administration. Research staff will ask teachers in both groups during the one week of PA data collection at baseline and each follow-up assessment timepoint to record if any children did *not* participate in MTI using a log developed and used during our pilot. Research staff will visit classrooms daily during PA data collection weeks to obtain this information from the teachers if they were not able to log the data. The time stamp of accelerometer data and data on each student's schedule on occurrence of recess, PE, field trips, MTI or other activity during each data collection time point will allow us to better determine when PA is occurring for most children.

COVID-19 Contingency Plan:

- In the event of school closures, students being on exclusive remote learning or research staff restriction in visiting schools, we will use procedures recommended and used during COVID-19 pandemic in adult patients with diabetes (who are at higher risk of COVID-19) by our study consultant (expert in physical activity assessment, Dr. Alex Rowlands): We will mail accelerometers that have been previously sterilized with alcohol/disinfectant wipes to participant's home. We will include sterilization kit (gloves and wipes) for participants to sterilize the devices again. Participants will be instructed not to open the envelope for two days after receipt to further minimize the risk of infection/spread (based on the virus only surviving in hard surfaces for about 2 days).
- We will email the log to the teachers in participating classrooms and follow-up with them to receive the information about MTI participation or any PE class that students may have participated when in school.
- We will also mail the log to child's home to record time child put on/removed monitor and any activity he/she participated during the week of data collection.

If research staff will be allowed to visit schools or parent requests to meet research staff to deliver or pick up an accelerometer or deliver a peak flow meter, the staff will meet parent in a public location, outside, or leave the devices in front of the participant's home/door and use standard precautions (wearing a face mask, practice social distancing, using gloves) to pick up/deliver the devices.

Body Mass Index (BMI) percentile and BMI z-score: With the asthma-obesity link[119] and potential effect of PA on weight, we will use digital scale and stadiometer to measure height and weight at baseline and 9 months[120] using scales/stadiometer that are available in school nurse office.

COVID-19 Contingency Plan:

- If students are on a hybrid model learning, we will ask the school nurse (or clinic staff at the Montefiore School Health Program) to obtain the height and weight of students enrolled in the study.
- Alternative method of obtaining BMI: We will ask caregivers (for those who have scales/tape measure at home) to provide this information at specified time points. If the scales/tape measure is not available at family's home, we will ask if parent has information on child's weight and height obtained at the most recent PCP appointment. Finally, for participants who are patients of Montefiore, we will obtain BMI information from the Epic medical records or request this information from the child's PCP.

- Permission to review medical record data will be obtained during informed consent process from the caregiver (and child ages 7 years and older)

In collaboration with the Office of School Health (DOE/DOH) and schools (with parental and child permission), we will request the school/DOE to provide data on enrolled students' school attendance record during the study period, physical education (PE) schedule, enrolled students' participation in any physical activity at school, school nurse visits, height and weight on file (for BMI calculation), medication use, and academic performance. This data is not available at this time; parents and students have not been enrolled and data will not be available until all enrolled students complete the study. A formal data sharing request will be submitted at a later time; agreements and approval letters for collection of existing human subject data will be submitted then as well.

Process Evaluation: We will use *RE-AIM* framework at the end of each study year to assess: **(1)** the proportion of eligible subjects who participate and the representativeness of participants compared to non-participants **(*Reach*)**; **(2)** the intervention's impact on primary (SFDs) and key secondary (PA) outcomes. We will also explore potential mediators and moderators of intervention effects ***(Effectiveness)***; **(3)** characteristics of schools and program support by school administration, PCPs, and students/caregivers ***(Adoption)***; **(4)** the consistency in intervention delivery (% completed education sessions by CHWs; # MAFs filed with school and rescue medication availability; visitation of classrooms and participation checklists in both Asthma-PASS and AM schools for student PA participation and report of participation in other PA activities); environmental and system barriers to *Asthma-PASS* implementation; and adequacy of resources. We will also collect data on the cost of intervention implementation for future planning of a formal cost-effectiveness analysis **(*Implementation*)**; and **(5)** the extent to which intervention components were continued or modified post-study completion in the context of available resources in city schools to facilitate dissemination to other schools ***(Maintenance)***. We will critically evaluate barriers and facilitators of sustainability in resource-poor schools. The final interview will include Likert-scale and open-ended questions to children, parents, PCPs, school personnel about convenience, scheduling, sustainability, and satisfaction.

Summary of Analytic Plan:
We will use graphical and numerical summaries to describe the outcomes at each assessment point. If distributional assumptions associated with particular statistical procedure are violated, appropriate transformations will be made or non-parametric tests will be used. All randomized participants will be analyzed within the group to which they were assigned as per the intent-to-treat principle. Hypothesis-driven comparisons will be made to control the type I error rate at 0.05 (two-sided) for the primary hypothesis.

Specific Aim 1: ***Examine the effectiveness of the Asthma-PASS intervention in reducing asthma morbidity.*** **Hypothesis 1a (primary):** Children in schools randomized to *Asthma-PASS* will experience a greater improvement in the number of SFDs at 3, 6, 9, and 12 months than AM comparison group. **Hypothesis 1b (secondary):** Children in *Asthma-PASS* group will have a greater improvement in asthma control (assessed with Childhood Asthma Control Test), quality of life, and pulmonary function, and less health care utilization at 3, 6, 9, and 12 months compared to asthma management (AM) comparison group.

Preliminary Analysis
We will determine whether there are differences at baseline between the *Asthma-PASS* intervention and AM groups in demographics and background characteristics (age, race, ethnicity, caregiver education), asthma severity/control and BMI. We will employ the generalized linear model (GLM) for this comparison and generalized estimating equations (GEE) to account for the within cluster correlation due to cluster sampling.

Primary Analysis (Specific Aim 1, Hypothesis 1a)
The primary aim of this study is to determine the effectiveness of the *Asthma-PASS* intervention. In the primary analysis, we will compare the change from baseline to each of the four post-baseline assessment (3, 6, 9, and 12 months) on number of SFDs (in past two weeks) between *Asthma-PASS* and AM children. If any of those four comparisons are found to be significant, we will declare the intervention is beneficial as the effect at 3-month, 6-month, 9-month, and 12-month follow up represents the immediate, short-term, intermediate, and long-term effects respectively. The Holm step-down procedure[121] will be used to adjust for multiple

comparisons. The primary null hypothesis is that the change over time on number of SFDs will not differ among those randomized to *Asthma-PASS* intervention or AM group. To test this hypothesis, we will follow the intent-to-treat principle. In particular, all randomized participants will be analyzed in the group to which they were assigned irrespective of their post-randomization behavior, and all participants randomized will be analyzed (using multiple imputation techniques). We will employ the generalized linear model (GLM) with identity link function for this comparison. The primary analysis model is of the form $EY=\alpha+\beta I+\sum\gamma_j T_j+\sum\delta_j IT_j$, where Y is the number of SFDs, I denotes group indicator for *Asthma-PASS* group (vs. AM), and T_j is the indicator of assessment time at j months (vs. baseline) for j=3, 6, 9, and 12 months. The regression coefficient δ_j corresponding to the group-by-time interaction term estimates the difference in average change of SFDs in past two weeks at j months vs. baseline, comparing intervention to AM group, and thus represents the effect of intervention on the primary outcome at j months. We will use GEE methodology to account for within-subject correlation due to multiple assessments for the same subject as well as the within-grade and within-school correlations due to cluster sampling.[122] Assuming no significant group differences in participant characteristics, the primary analyses will be those described above. If there are any significant group differences in participant characteristics at baseline such as gender, race/ethnicity, socioeconomic status, number of comorbid conditions, asthma severity, potential motivation towards child's physical activity that may influence the primary (and secondary) outcomes, we will include such variables in the regression models to adjust for potential confounding and report the adjusted intervention coefficients as the primary result.

Secondary Analysis of Other Asthma Measures (Specific Aim 1, Hypothesis 1b)
In the additional analysis, we will test for differences between *Asthma-PASS* and AM groups on the change over time in asthma control (assessed with Childhood Asthma Control Test), quality of life and pulmonary function. The analytic approach will be the same as for the primary analysis. However, we will use identity link function for continuous variables (such as symptom days and nights, days absent from school, quality of life, cACT and ACT scores, and FEV1), and logit link for dichotomous variables (such as rescue medication use). We will also compare the occurrence of acute visits and/or hospitalizations between the two groups via GLM with logit link with GEE to account for the within cluster correlation.

Missing Data
Our previous study demonstrated an excellent retention rate (**one year retention rate was 96% for children and 91% for parents**) and we anticipate the retention rate will be as good in this study. With such a high retention rate, the impact of missing data should be minimal. However, we will still try our best to minimize participant drop-out from the study. We will balance the competing goals of reducing participant's response burden with collecting sufficient information to fully support the analytic goals of the trial and to guide the next steps in intervention. Study coordinators will send out reminders (phone calls or text messages) prior to scheduled visits and will call the participants if they do not complete their scheduled assessment. We will provide modest incentives for study participation (as described in the ***Outcomes Assessment*** section). If participants become dissatisfied with participating in the study but have not yet withdrawn, we will make every effort to address their concerns and retain them in the study to avoid the participant's dropping out. We will state and restate the importance of their continuing participation for follow-up purposes and their valued contribution to the research of pediatric asthma. For participants who miss follow-up assessments, coordinators will attempt to determine whether they are just unavailable on that day so that they can reschedule the assessment, or whether there are other reasons that prevent their continued participation (e.g., moving out of the area). If a participant entirely withdraws their consent to be followed up, we will attempt to determine the reasons for their dissatisfaction, and will use those reasons to help build a clinically informed and reasonable imputation plan for their missing outcomes (see below). Rubin's multiple imputation method with 11 repeated imputations will be employed to impute the missing endpoint for conducting the intent-to-treat analysis.[123] We will use a statistical imputation model using all available baseline and post-baseline assessments in a pooled analysis (i.e., blind to intervention assignment) which is unbiased under the null hypothesis.

As explained above, every effort to retain participants in the study will be exerted in order to avoid attrition. For each participant who wishes to terminate his or her participation in the trial, the study coordinator will document their reasons for study discontinuation in a trial participation discontinuation report form and trial close-out form which will be collected and maintained by the research team. The intent-to-treat principle (analyze participants in their randomized assignment groups and "once randomized, then analyzed") will be followed. A strength of

Rubin's multiple imputation procedure is that it allows all available information from all randomized participants to enter the analysis.[123] We will conduct sensitivity analyses to evaluate how robust the study inferences are to missing data.

Subgroup Analysis

In addition to the primary comparison on the primary outcome (SFDs) between participants in *Asthma-PASS* intervention and those who assigned to AM for all study participants, we will also evaluate the intervention effect by gender and by race/ethnicity. For each of these pre-specified subgroup analyses, in addition to evaluating the intervention effect separately within each subgroup, we will also examine the effect modification by fitting a model with intervention indicator, time indicators, subgroup indicator, and their 2-way and 3-way interaction terms. As the regression coefficient corresponding to the 3-way interaction term represents the difference of the intervention effects between the subgroups, this approach will allow us to test the statistical significance of differences in intervention effects between pre-specified subgroups. Statistical significance for interaction effects will be declared at the 5% level.

Specific Aim 2: ***Assess the effectiveness of Asthma-PASS on increasing PA levels.*** **Hypothesis 2a and 2b (major secondary):** a) A greater proportion of children in *Asthma-PASS* will participate in in-class PA, and b) Children in *Asthma-PASS* will have higher overall levels of PA, compared to AM.

Major Secondary Analysis (Specific Aim 2)

In this major secondary analysis, we will evaluate the *Asthma-PASS* intervention effect on PA outcomes by comparing (a) proportion of children participating in in-class PA and (b) the improvement over time in minutes of PA between intervention and AM group participants. We will also evaluate the impact of *Asthma-PASS* on both in-school PA (classroom, recess, PE class) and out-of-school PA. To test Hypothesis 2a we will use GLM with logit link function and GEE methodology to account for within-grade and within-school correlations due to cluster sampling.[122] The analytic approach for testing Hypothesis 2b will be the same as that used for the primary analysis.

Power Analysis

With a recruitment of 416 students at baseline, we anticipate a final sample of 374 participants with complete data for the primary analysis assuming no more than 10% attrition at the final follow-up. This estimate of attrition rate is conservative as our pilot work demonstrated a greater than 90% retention rate at one-year after intervention (96% retention rate for children and 91% for parents). To account for the intra-cluster correlation due to cluster sampling, we used the intra-grade correlation coefficient of 0.03 estimated from our pilot data. Although the intra-school correlation coefficient should be smaller than intra-grade correlation coefficient, we conservatively used the same value (i.e., 0.03). With that assumption, the inflation of standard error due to cluster sampling is then by a factor of vif=1+(ng-1)*iccg+(ng*ns-1)*iccs where ng and ns are weighted average cluster size within grade and within school respectively and iccg and iccs intra-grade and intra-school correlation coefficients respectively. As the planned enrollment for 6-8 grades per school (possibly from pre-kindergarten to 6) and at most 4 students per grade (depending on the size of school and eligible students for each grade), we use ng=2 and ns=7 for this power calculation. Using the following formula: standardized difference in change over time $d=(Z_{0.05/8}+Z_{0.2})$*(square root of ((2/n)*vif), with n=187 participants per group, we will be able to provide 83% power to detect a standardized effect size of 0.42 or more in change of number of SFDs with Bonferroni adjustment for multiple comparisons for testing 4 primary hypotheses and accounting for the type I error inflation due to the interim analysis. This 0.42 standardized effect represents approximately 2 more SFDs improvement which is the "minimal worth-while effect size" we aim to examine, so it is critical to plan the study that provides adequate power to declare such effect as statistically significant. Note that we calculated the detectable standardized effect size for the ***change*** from baseline to each of the 4 follow-up assessments which is equivalent to the difference (between intervention and control) in change of SFDs (from baseline to follow up) divided by the standard deviation of the change score. As the standard deviation of the change score has imbedded the within subject correlation due to repeated measures, we properly accounted for the multiple assessments of the primary outcome in our sample size calculation. Furthermore, we ***purposely*** use a simpler and more conservative Bonferroni procedure to adjust for multiple comparisons in this sample size calculation as such approach not only assures an adequate power for the study even for multiple testing of dependent null hypotheses, it also provides cushion to guard against other unexpected

factors (such as unexpected higher rate of missing data, greater intra-class correlations, etc.) that can cause the loss of power. This power analysis applies to PA and other secondary outcomes as well. Furthermore, as we will impute missing data using informative covariates for the primary analyses and use a less conservative Holm step-down procedure for multiple comparison adjustment,[121] the power to detect such effects will actually be greater than 80%. For the gender and ethnicity subgroup analysis, the multiple comparison adjustment will only apply to the 4 comparisons within each subgroup rather than all 16 comparisons. We anticipate a 50%-50% to 30%-70% split between the two subgroups (i.e., male vs. female or Non-Hispanic vs. Hispanic) and the proposed sample size will allow us to declare a moderate to large standardized effect size (0.60 to 0.92) as statistically significant with 80% power.

Specific Aim 3: ***Identify intervention mediators and moderators.***
In Specific Aim 3, we will determine whether or not enhanced knowledge, beliefs/attitudes, self-efficacy, medication adherence, outcome expectancy, and PA levels, mediate the effect of intervention on outcomes. Mediation analysis will be conducted using the test of joint significance of the 2 paths involving a potential mediator, which best balance Type I error and statistical power.[126] A variable M (e.g., PA level) will be declared a mediator if and only if both the test of the regression coefficient of the explanatory factor X (i.e., the *Asthma-PASS* intervention indicator) on the mediator AND the test of the coefficient of the mediator on the outcome variable Y (i.e., SFDs) controlling for X are both significant at level alpha=0.05, two-tailed. This approach allows for partial mediation which we expect to occur (as opposed to total mediation). In subsequent analyses we will estimate the indirect path effect with 95% confidence intervals using the asymmetric distribution of products method.[126] Further exploration of causal mediation will follow the methods of Imai et al.[127] We will also examine whether the demographic and school/neighborhood characteristics will moderate the effect of intervention. The statistical model will include the potential moderator, *Asthma-PASS* intervention indicator, time indicators, and all the two-way and three-way interactions. If the regression coefficient corresponding to the three-way interaction term is statistically significant, we will report the intervention effects for each of the corresponding subgroups.

Specific Aim 4: ***Evaluate the process of intervention implementation.***
We will use descriptive statistics and bivariate comparisons for the process evaluation, looking in particular at the efficiency of program implementation along with responses from parents, PCPs, and school staff about convenience, scheduling, satisfaction, and sustainability. We will evaluate RE-AIM[128] metrics to assess generalizability and reach. To estimate *Reach* we will determine the proportion of eligible children with asthma who participate in the study, and will use data from screening forms to characterize differences between those who participate and those who do not. To estimate *Effectiveness*, we will conduct intent-to-treat analyses of the primary (SFD) and secondary (PA) outcomes. We will use school data and interviews from participating parents and children, key school and community members to evaluate *Adoption*. We will conduct interviews following the intervention to gauge their reaction to the intervention components and their willingness to support them in the future. To assess *Implementation* we will use check-lists and tracking logs to measure the extent to which participants partook in each program component. To assess *Maintenance* we will use survey responses to evaluate the extent to which each intervention component was continued or modified post-study in the context of available resources in city schools. Long-term intervention effects at 12 months will be analyzed as described above in the analysis of primary/secondary outcomes. We will evaluate barriers and facilitators of sustainability in resource-poor schools by interviewing parents, PCPs, and school personnel about convenience, scheduling, sustainability, and satisfaction. The final interview will include Likert-scale and open-ended questions.

PROTECTION OF HUMAN SUBJECTS

Potential Risks (See DSMP for additional details on potential risks and safeguards to protect against risks)
This is ***not*** a drug investigational study since the effectiveness and safety of the drugs are not being tested. The randomized trial proposed will pose minimal risk to the children. To measure physical activity, we will use an accelerometer to record physical activity levels (duration, frequency, and intensity) of students with asthma. There are no risks involved for students to wear this device. We have used this device in 109 children enrolled in our pilot study, approved by both NYC DOE IRB and Einstein/Montefiore IRB. We will use accelerometer

device sterilization procedure currently being used in other physical activity studies and provided by our expert (Dr. Rowlands). The only risks involved are those of Move-to-Improve, the NYC DOE-endorsed daily activity program that students normally would have if they are to participate in the school physical education classes. For this purpose, the usual safeguards that the schools are using will be employed, including prior medical clearance from a physician for sports participation.

There is no risk in measuring FEV1 as each child participant will receive their own device to use throughout the study or come to the clinic to have this assessment.

It is possible that some students with more severe asthma or poorly controlled asthma may experience asthma symptoms due to participation in the MTI. The MTI is similar to our previously evaluated CHAM JAM program, which is based on an interval training approach with periods of more intense exercise alternating with less intense activity. This method is more characteristic of the spontaneous PA in children and has been found to improve endurance and tolerance capacity to exercise stimulus in children with EIA. In our pilot study involving 109 students, as well as in prior study evaluating CHAM JAM effectiveness with over 10,000 Bronx elementary school students, there were no reports of injuries or students developing asthma symptoms requiring school nurse or physician visits due to participation in CHAM JAM. Any concerns related to study participation will be relayed promptly to the child's PCP, the study coordinator, and the principal investigator, as well as the Institutional Review Board, the Data and Safety Monitoring Board (DSMB), and the NIH.

We will be collecting confidential information about asthma diagnosis, school nurse visits for asthma, age, ethnicity and race, class code and school identification number. A Data Use and Non-Disclosure Agreement between the New York City Department of Health and Mental Hygiene/NYC DOE and Montefiore Medical Center has been signed to securely transfer, store, and use data on school nurse visits in our pilot study using safeguards to protect data confidentiality. The same agreement will be executed to obtain school nurse visit data for participants in the proposed study.

By participating in the surveys, students and parents may lose time that could have been used for other activities. Potential risk may also include loss of privacy during height and weight measurements.

Protection Against Risks
Human subjects' rights will be protected as explained in the consent forms used for the study. The Montefiore/Einstein Institutional Review Board (IRB) and the NYC DOE IRB will review the protocol, informed consent documents, survey instruments, and other study-related materials. Research will be carried out only after proper approval from both IRBs.

We will obtain informed consent from the parent. Assent will be obtained from all children ages 7 and older after parent agrees for the child to participate. Informed consent will be obtained from all study participants by research personnel trained and certified in human subjects protection. The informed consent process will detail the information about who is conducting the study, the purpose of the study, the procedures (including randomization, the number of surveys and intervention description, etc.), study potential benefits and risks, a discussion of compensation, data confidentiality, and a statement that participation is voluntary. All oral explanations and written consent forms will be IRB and HIPAA compliant. Participants will be informed that they may choose not to answer any of the questions on the surveys and not to provide FEV1 or accelerometer measurements, and that they may withdraw from the study at any time without negative consequences. Strict confidentiality will be maintained throughout the study. All data will be stored in locked file cabinets in the PI's study office. Only the researchers or their associates will have access to these data.

Consent for study participants and their classmates to participate in the MTI exercise component of the intervention is not required as schools endorse it as a routine part of the school day. In addition, no data will be collected from classmates.

All data collected will be confidential and will be used only for research purposes. Since the study is geared toward students with asthma and personal health information about the diagnosis of asthma to identify eligible

participants is part of the study, every precaution and safeguard will be taken to protect confidentiality of participants. The following data management procedures will be performed to minimize the risks of breaching confidentiality: 1) All surveys collected that contain information about asthma diagnosis will be stored in secure and locked cabinets in the PI's locked office; 2) Using only pre-assigned ID numbers with no other identifying information; 3) Storing the master list with ID codes and names separately in a locked drawer; 4) Storing consent forms in separate lockable file cabinet; and 5) All electronic data files will be password protected limiting to project staff's access only. To further protect research participants' identities, we will de-identify the data by removing the following variables and use pre-assigned ID numbers with no other identifying information: 1) Participants' names; 2) Geographic information (city, state, zip code); 3) Date of birth; 4) Telephone numbers and home addresses; 5) School and classroom codes.

REDCap (Research Electronic Data Capture)

REDCap is a secure web application geared to be used by research studies to build and manage online surveys and databases. We will use REDCap to collect baseline and follow-up survey data. REDCap survey systems provide secure, web-based applications that are flexible enough to be used for various types of research, provide an intuitive interface for users to enter data, and have real-time validation rules (with automated data type and range checks) at the time of entry. REDCap servers are housed in a data center at Einstein and all web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines and is recommended to researchers at various institutions by both Privacy Offices and Institutional Review Boards. REDCap has been disseminated for use locally at other institutions and currently supports over 3500 institutions in 130 countries and over 970,000 research end-users (www.project-redcap.org).

Additional Measures to Protect the Data:

We will take additional measures to minimize the risk of breaching the confidentiality of data. These include but are not limited to the following:

- Electronic firewalls
- Audit trails
- Disaster prevention and recovery plans
- Systems certification
- All research personnel take yearly HIPAA training

Identity of participants will not be revealed in the presentations or publications of any results from the project. All personnel working on the project will be regularly educated about the importance of strictly respecting participants' rights to confidentiality. As all the coding will be de-identified, and study results reported in aggregate means, there will be minimal risk to all participants.

All NYC public schools with a student population over 200 have a nurse during school hours. Each of the identified schools has a nurse on-site who is available to clinically assess any student with asthma symptoms when students are attending school in-person. The nurse will have contact information for the PI and will be asked to refer the child for medical care and inform the PI and the school principal immediately of any adverse events (asthma symptoms and other injuries) related to the Move to Improve participation. Additional safeguards will be implemented for students who will be participating in Move to Improve (MTI), NYC DOE activity program or another physical activity (CHAM JAM), if these have to be carried out remotely (via Zoom) by research team if schools close or children attend school remotely and teachers are unable to deliver the program during the school hours as part of routine class activity: 1) prior to initiating the CHAM JAM activity with the child, the study team member will confirm with the parent that child does not have acute asthma symptoms or COVID-19 symptoms; if the child has such symptoms, they will be excluded from participation that day and parent will be instructed to refer to asthma action plan or seek urgent medical care for severe symptoms; 2) requiring that an adult caregiver is present with a child at the time of physical activity; 3) availability of asthma rescue medication at home; 4) for children with exercise-induced asthma, encouraging the use of pre-exercise rescue medication; 5) instruction to stop physical activity if having symptoms; 6) instruction to refer to asthma action plan or seek urgent medical care for severe symptoms, and 7) contact PI and research staff to inform of the event associated with physical activity.

To minimize potential discomfort and assure student confidentiality, anthropometric measures will be taken behind a screen or in a nurse's office in a private manner, with children in indoor clothing and shoes off. Participants may opt out of the study at any time if they choose.

Any child experiencing an exacerbation during the encounter with study staff in either intervention or comparison group will be immediately referred to their asthma action plan provided by child's PCP for home use and if asthma action plan is not available, they would be referred to their PCP/urgent care clinic or ED for care. For students without a PCP, we will refer families to one of Montefiore Medical Center's 20 group practices that are situated throughout the Bronx. For students whose parents do not have medical insurance or who are unable to go to a Montefiore clinic, the New York City Department of Education (NYC DOE) physicians, who routinely attend at NYC schools, will provide medical care and prescribe appropriate asthma medications.

The research assistants will make efforts to protect subject privacy and confidentiality. The research assistants will ensure that the subject is comfortable answering questions and discussing the study prior to completion of consent or any study measures. If it is suspected that someone in the home may cause serious harm to themselves or others, the study team will report these issues to the Sr. Project Coordinator and the principal investigator who may be mandated to report these concerns to appropriate authorities. There is also a risk that the study team may discover an unknown medical condition. If this is to occur, we will refer the family to their PCP or another appropriate health care professional for evaluation and treatment.

Safety Measures: The frequency and severity of all adverse events will be systematically recorded. There were no adverse events related to pilot study participation. If any child develops asthma symptoms during MTI, he/she will be immediately evaluated by a school nurse as per school protocol for those children who are physically in school. Any child (in either group) experiencing an asthma exacerbation during a study session or assessment will be referred promptly to their PCP/ED for care. Any concerns related to study participation will be relayed promptly to the child's PCP, the study coordinator, and the principal investigator, as well as the Institutional Review Board, the Data and Safety Monitoring Board (DSMB), and the NIH.

Costs:
Because the treatments are standard of care for children with persistent or uncontrolled asthma, participants and their insurance plans will be responsible for the costs of medications and spacers during the study, including those used at school. New York City schools have stock quick reliever (Albuterol Sulfate) inhalers available for shared use as long as the MAF is completed by child's physician and filed with the school. Schools also have spacers to provide to students to use in school. Based on our prior work with this population, we anticipate that most of the children will have health insurance to cover the costs of medications with minimal or no co-pay fee. If a child (in either group) does not have insurance, the study team will help the family secure health insurance.

POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO HUMAN SUBJECTS AND OTHERS
Given the minimal risks associated with our intervention, we believe the benefits outweigh the risks. As a whole, we believe this study will ultimately benefit the students. All students in the intervention schools will participate in a school-wide asthma awareness week with the ultimate goal of eliminating stigma around asthma.

By participating in *Asthma-PASS,* children and caregivers will receive asthma education that will teach them the importance of managing asthma to promote physical activity, address fears about asthma and physical activity, and medication adherence to control symptoms and enable physical activity. Children in the AM comparison group will receive basic asthma education and the PCPs of these children we be notified to assure that the appropriate asthma medication regimen has been prescribed as per guideline-based care.

We also believe this program will provide benefits to school personnel, including classroom teachers, PE teachers, and recess aides in the intervention group. The school personnel will be offered an asthma education

workshop. The workshop includes a didactic session on recognizing asthma symptoms and handling an asthma attack in school, promoting communication between parents, teachers, and school nurses, and creating an asthma-friendly classroom environment. The workshop will focus on encouraging student PA participation and address the lack of knowledge associated with asthma and physical activity, thereby promoting teachers to encourage their students with asthma to participate in physical activities. This education may improve asthma management at the schools, ultimately benefiting the students. School personnel participate in yearly professional development workshops mandated by the NYC DOE. This workshop will provide a certificate of completion which may be used towards professional development.

Compensation

Schools will receive up to $1,000 donation to purchase equipment for physical education or other student supplies. Teachers of participating students will receive $50 reimbursement for classroom supplies for their participation in collecting screening forms, completing logs during student activity assessments, and for providing feedback about convenience, scheduling, sustainability, and satisfaction as part of the process evaluation.

Caregivers will receive $20 at baseline, $15 after each follow-up phone survey, and $35 at study completion (up to $100 total for the entire study period). We will use ClinCards to provide parent payments. The ClinCard, produced by Greenphire, is an automated, reloadable payment card which can be used like a credit card for in-store and online purchases, or cash advances. Children will receive $10 gift card at baseline and each time they wear the accelerometer (3, 6 and 9mo follow-ups) (up to $40 total for the entire study period), and a toy for survey completion. The amount of compensation to the study participants is well within the Montefiore-Einstein IRB Guidelines for Compensation of Research Subjects.

IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Physical activity is an important component of pediatric asthma management and has been shown to improve asthma outcomes; however, urban minority children with asthma face many barriers to participation in sports and other forms of physical activity. The goal of this proposed intervention is to determine effectiveness of an innovative, school-based intervention, *Asthma-PASS.* This intervention supports guideline-based asthma management through collaboration with PCPs and utilizes Community Health Workers to facilitate care and deliver targeted education, reducing asthma morbidity and improving physical activity in elementary school-age children with persistent or uncontrolled asthma. This study is important as it targets asthma, a common childhood disease disproportionately affecting urban minority children. Few interventions have been tested in schools for this population – this intervention addresses barriers to physical activity at the child/family, school, and health system levels. *Asthma-PASS* was developed in collaboration with parents, teachers, and NYC school officials to assure it would be acceptable and ultimately sustainable.

The current study may have a profound impact on public health because it aims to rigorously evaluate the effectiveness of an integrated, novel, school-based intervention that addresses key barriers to physical activity in urban minority children with asthma. Should the intervention prove successful in reducing symptoms and improving health of urban children with asthma, it has the potential to serve as a model for improved asthma care in urban communities.

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