The Development and Pilot Testing of a Caregiver-Child Shared Decision-Making Intervention to Improve Asthma in Urban Youth

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1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: **The Development and Pilot Testing of a Caregiver-Child Shared Decision-Making Intervention to Improve Asthma in Urban Youth**

Grant Number: **1R21NR019668**

Study Description: This is a feasibility trial of a brief shared decision-making intervention that primary care providers will deliver to caregivers and their children aged 10-14 during a routine office visit, focusing on improving self-management. Brief shared decision-making will be compared to a dose-matched attention control; providers will be randomized to deliver either the active (n = 43) or control (n = 42) intervention to dyads (N = 85) who will be followed for 3-months. The trial will be informed by focus groups (caregivers separately (n =20) ; early adolescents separately n =20) and dyads (n =20) (N=60).

Objectives:

1. **To develop BREATHE-PEDS in a pediatric population (dyads of caregivers and their 10- to 14-year-old early adolescents with uncontrolled asthma) receiving asthma care in FQHCs;**
2. **To evaluate the feasibility and acceptability of intervention procedures; and**
3. **To assess intervention effects on asthma outcomes (monthly x 3 months post-intervention).**

To accomplish these aims the proposed study includes two phases: (1) a development phase where we will develop **BREATHE-PEDS** using focus groups. Participants (N = 60) will include early adolescents (n = 20), caregivers (n = 20) and dyads (n=10 dyads) to adapt **BREATHE-PEDS**, and (2) a pilot validation phase where we will conduct a group-randomized trial in two FQHCs with 85 dyads treated by 8 PCPs (10 dyads/PCP) randomized to 1 of 2 study arms: (a) **BREATHE-PEDS** (n=42 dyads), or (b) dose-matched attention control (n=43 dyads). We will conduct post-trial interviews with PCPs, caregivers, and their children to evaluate satisfaction with the intervention; we will follow caregiver-child dyads for 3 months post-intervention to assess the impact of **BREATHE-PEDS** on asthma outcomes.

Hypotheses:

1. The intervention will be feasible and acceptable as evidenced by: high rates of dyad recruitment and retention; PCP fidelity to the intervention protocol; and PCP and caregiver-child dyad satisfaction.
2. Over 3-months post-intervention, relative to controls, **BREATHE-PEDS** children will have improvement (a) in asthma control as measured by the *Asthma Control Questionnaire*[63-65] (primary outcome), higher perceived SDM, and (b) on other asthma outcomes (secondary outcomes), including quality of life, school absences, lung functioning, and exacerbation.

Endpoints:

NAME: Asthma Control Questionnaire
TYPE: Primary
TIME FRAME: Focus groups, Baseline and 1-, 2-, and 3-months post intervention
DESCRIPTION: 6-item validated and widely used measure of asthma control
WHO COMPLETES: Child with help from caregiver as needed

NAME: Shared Decision-Making Questionnaire– 9 items
TYPE: Secondary
TIME FRAME: Focus groups, Immediately after the medical visit (i.e., immediate post-intervention)
DESCRIPTION: 9-item validated measure of the decisional process in medical visits from both patients' and physicians' perspectives
WHO COMPLETES: Child AND Caregiver (PATIENT version) and PCP (clinician version)

NAME: Medication Adherence Record Scale-Asthma
TYPE: Secondary
TIME FRAME: Focus groups, Baseline and 1-, 2-, and 3-months post intervention
DESCRIPTION: 10-item validated measure of inhaled corticosteroid adherence (ICS) (dichotomized as high or not). Scores have been shown to predict Self-management as measured by objective electronic monitoring and prescription refill rates.
WHO COMPLETES: Child with help from caregiver as needed

NAME: Conventional and Alternative Management for Asthma
TYPE: Secondary
TIME FRAME: Focus groups, Baseline and 3-months post intervention
DESCRIPTION: 17-item validated measure of erroneous asthma management beliefs (9 items) and ICS beliefs (8 items)
WHO COMPLETES: Child with help from caregiver as needed AND Caregiver

NAME: Pediatric Asthma Quality of Life Questionnaire
TYPE: Secondary
TIME FRAME: Focus groups, Baseline and 1- and 3-months post intervention
DESCRIPTION: 23 questions in 3 domains (symptoms, activity limitation and emotional function). The activity domain contains 3 ‘patient-specific’ questions. Children are asked to think about how they have been during the previous week and to respond to each of the questions on a 7-point scale (7 = not bothered at all -
1 = extremely bothered). The overall PAQLQ score is the mean of all 23 responses and the individual domain scores are the means of the items in those domains
WHO COMPLETES: Child with help from caregiver as needed

NAME: Pediatric Asthma Caregiver's Quality of Life Questionnaire
TYPE: Secondary
TIME FRAME: Focus groups, Baseline and 1- and 3-months post intervention
DESCRIPTION: 13-item in two domains (activity limitation and emotional function). Parents recall the impact that their child's asthma has had during the previous week and score each question on a 7-point scale.
WHO COMPLETES: caregiver

NAME: Asthma Impairment and Risk Questionnaire (AIRQ) BASELINE
TYPE: Secondary
TIME FRAME: Focus groups, Baseline and 1-, 2-, and 3-months post intervention
DESCRIPTION: 10-item valid and reliable survey that measures both domains of control: symptom impairments and risk for uncontrolled asthma
WHO COMPLETES: Children aged 12 and older

NAME: Asthma Impairment and Risk Questionnaire (AIRQ) FOLLOWUP
TYPE: Secondary
TIME FRAME: 1-, 2-, and 3-months post intervention
DESCRIPTION: 10-item valid and reliable survey that measures both domains of control: symptom impairments and risk for uncontrolled asthma
WHO COMPLETES: Children aged 12 and older

NAME: Brief debriefing survey
TYPE: Secondary
TIME FRAME: Immediately after the medical visit
DESCRIPTION: 10-item (caregiver) and 5-item (PCP) yes/no/short answer survey that asks the participant to recount what happened at the visit
WHO COMPLETES: Three versions Caregiver, Patient AND PCP

NAME: Asthma exacerbation
TYPE: Secondary
TIME FRAME: 1-, 2-, and 3-months post intervention
DESCRIPTION: Oral steroid use 1 year pre- through 1-year post-intervention; report of asthma-related acute care visits, ED visits, and hospitalizations; or Intensification of bronchodilators (to be defined by SMC). All self-reported and/or extracted from provider notes in the electronic health record, confirmed by claims data where available.
WHO COMPLETES: Child and Caregiver

NAME: Asthma Responsibility Questionnaire

Miscellaneous:

TYPE: Secondary
TIME FRAME: Focus groups, Baseline and 1- and 3-months post intervention
DESCRIPTION: 10-item validated measure assessing who is responsible for various asthma care tasks
WHO COMPLETES: Child and Caregiver

NAME: Newest Vital Sign
TYPE: Other
TIME FRAME: Focus groups, Baseline
DESCRIPTION: 6-item validated and widely used measures of health literacy
WHO COMPLETES: Caregiver

NAME: Short Assessment of Health Literacy-Spanish and English
TYPE: Other
TIME FRAME: Focus groups, Baseline
DESCRIPTION: Validated measures of health literacy
WHO COMPLETES: Caregiver

NAME: Asthma Prevention Index
TYPE: Other
TIME FRAME: Baseline and 1-, 2-, and 3-months post intervention
DESCRIPTION: 11 item index measuring how many steps and the regularity in which the steps are taken to prevent symptoms from occurring.
WHO COPLETES: Child and Caregiver

Asthma history (e.g. age at diagnosis); Demographics
TYPE: Other
TIME FRAME Baseline
WHO COMPLETES: Caregiver

Study Population:

Aim 1: Focus groups (pre-trial). We will enroll caregivers (n =20) ; early adolescents (n =20) and dyads (n =10) (N=60) into separate focus groups.
Aims 2 & 3: Group-randomized trial. We will recruit 85 dyads and 8 clinicians to the trial.
Aims 2 & 3: Post-trial interviews. We will do post-trial interviews with a purposive sample of ~6 participating clinicians, ~10 early adolescents, and ~10 caregivers.

Inclusion of Women.
Caregiving participants in focus groups and the group-randomized trial. We anticipate enrolling more female caregivers than men because more women serve in the caregiving role. We therefore estimate that ~75% of our caregiving participants in this trial will be female. We will explore if there is a differential intervention effect by sex.

Provider participants (group-randomized trial). Based on the sex of the clinicians working at these sites, we anticipate that 75% of our 16 clinicians will be female.

Inclusion of Minorities.
Patient participants in focus groups and the group-randomized trial. Asthma prevalence and morbidity is increased in Latino (defined as a person of Cuban, Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race) and Black (defined as a person having origins in any of the black racial groups of Africa) youth. They also have more asthma-related emergency department (ED) visits and hospitalizations. To address these health disparities, we have partnered with Urban Health Plan, Inc. (UHP), a federally qualified health center (FQHC) that serves a predominantly Latino and/or Black community. Based on demographic data provided by UHP we anticipate that 95% of the adolescents will be ethnic-racial minorities with 85% Latino and 10% non-Hispanic Black; the racial/ethnic distribution of their caregivers is expected to be similar. Our team has extensive experience working in ethnically diverse populations, particularly in the context of asthma intervention research.

Provider participants (group-randomized trial). The racial and ethnic distribution of the PCP sample is expected to be approximately 50% Black, 45% White, 5% Asian, and 10% Hispanic; this is based on our prior experience with research involving FQHCs.

Post-trial interviews with clinicians, patients and caregivers. We will purposively sample to ensure a racial and ethnic diversity among our participants.

Other Vulnerable Populations.

	Pregnant women will be eligible to participate since improving asthma control for their early adolescent children would benefit the family.
Description of Sites/Facilities Enrolling Participants:	Participants will be recruited from 3 Urban Health Plan sites. They include: El Nuevo San Juan 1065 Southern Blvd Bronx, NY 10459 Adolescent Health and Wellness 960 Southern Blvd Bronx, NY 10459 Bella Vista 822 Hunt's Point Ave Bronx, NY 10474
Description of Study Intervention/Experimental Manipulation:	**BREATHE-PEDS** utilizes Primary Care Providers (PCPs) to deliver a brief tailored , shared decision-making intervention using motivational interviewing in a one-time 9-minute intervention during medical visits for asthma. PCPs will follow a 4-step script that was created by and tailored to black adults' asthma and inhaled corticosteroid beliefs, as well as their Asthma Control Questionnaire (ACQ) score, measured just prior to the medical visit. Step 1: Raise the subject (1½ minute). Step 2: Provide feedback (1½ minutes). Step 3: Enhance engagement (3 minutes). Step 4: Shared decision-making (3 minutes). Dose-matched Attention Control Condition. Control participants will receive a PCP-led 9-minute scripted discussion of healthy lifestyles (e.g., diet) following principles of Teach to Goal. Review of BMI, current diet and exercise: (3 minutes). Diet/exercise counseling: (3 minutes). Plan for goal attainment (3 minutes).
Study Duration:	Three months post intervention.
Participant Duration:	Pre-trial focus groups. One 2-hour session Group-randomized trial: Patient participants – 3 months Clinician participants = ~ 6 months (delivering the intervention one time to 12-13 patients during a single office visit) Post-trial interviews. One hour.

2 INTRODUCTION

2.1 STUDY RATIONALE

Uncontrolled asthma is an appropriate target for shared decision-making (SDM) interventions that support disease self-management as it is associated with higher asthma burden and worse clinical outcomes. To date, the application of SDM and community-based interventions targeting underserved communities have failed to address these disparities. Therefore, we will use patient and caregiver input to develop **BREATHE-PEDS - Brief intervention to Evaluate Asthma Therapy in Pediatrics** – a 9-minute SDM intervention focused on reducing the impact of erroneous beliefs on asthma control - and established its efficacy in this health disparity population. Our intervention is unique in that is a one-time brief, tailored intervention integrated into office visits, using the patient's own provider as the interventionist (e.g. scalable). Our pilot trial demonstrated high fidelity to **BREATHE-PEDS** delivery and

improved asthma control and reduced symptoms among adults compared to a dose-matched attention control condition.

This study addresses the important problem of uncontrolled asthma among a group at high risk for asthma and its adverse effects – urban minority children. Stakeholder-informed pragmatic trials are essential but are lacking in asthma intervention research. Our proposal addresses these weaknesses in the prior research.

2.2 BACKGROUND

A.1. Asthma's Impact is Significant in Minorities and Early Adolescents. Asthma is the most common chronic illness affecting 6 million US children[1]. Prevalence and rates of uncontrolled asthma are highest among Black and Hispanic youth[1-5]. Early adolescents (ages 10-14) have high asthma prevalence relative to younger children and adults[1]. Disability-adjusted life years (DALYs), a measure of asthma burden, peaks at ages 10-14[6-8], making asthma the third leading cause of DALYs[7] in this age group[6].
A.2. Early Adolescents have Poor Asthma Self-Management. Our team, and others, have demonstrated that early adolescents have sub-optimal asthma self-management, including trigger management and using medication preventively and when symptomatic[10-14]. Their poor self-management occurs in the context of unique developmental transitions that add challenges to self-management, including vulnerability to stress[13] and increased independence and autonomy[10,29,67], as well as opportunities to render them good self-managers due to the developmental gains they also make[68]. Yet, few interventions specifically target this age group. **A.3. Caregiver Engagement is Critical to Self-Management but is Lacking.** Despite the fact that a gradual transfer of responsibility to youth is recommeded[71], caregivers often prematurely expect their child to assume responsibility for their asthma self-management[72], with some transferring care as early as age 10[73]. Early adolescents often report having more responsibility for their asthma care than their caregivers[10,13], despite a desire to share responsibility[72]. Thus, caregiver engagement is critical for optimal asthma management during early adolescence[10,24,25]. Therefore, interventions are needed to engage caregivers to support their child's transition to independent self-management. Intervening with early adolescent-caregiver dyads has the potential for a synergistic effect improving asthma control beyond what an intervention for either alone might have.
A.4. Federally-Qualified Health Centers (FQHCs) are Optimal Settings for Asthma Interventions. Most (80%) asthma care is delivered by primary care providers (PCPs)[9], and uncontrolled asthma is more common in these settings compared to specialty care[74]. FQHCs are unique primary care settings providing asthma care for a greater proportion of minority patients with uncontrolled asthma[54]. There are unique challenges to achieving asthma control in FQHCs: their clients live in - or near - the US poverty level[54] and PCPs in FQHCs have limited time and resources[75] to evaluate asthma control and to identify suboptimal self-management. This speaks to the pressing need for novel brief interventions integrated into clinical care.
A.5. Tailored SDM Interventions Can Promote Asthma Self-Management. The study is guided by the evidence-based model, Shared Decision-Making (SDM)[76], which posits that the best treatment decisions are informed by *patients' preferences*, the best available *scientific evidence*, and *clinician expertise*. PCPs facilitate discussions of risks and merits associated with options in the context of patient's goals and preferences, and in a manner that activates patients to engage in self-management[51]. The goal of SDM is to reach mutually agreed upon higher quality decisions that align patient's self-management decisions with guideline-directed evidence-based care[77,78]. We have shown that SDM improves asthma control in adults[30,53], and SDM has been used in other areas of pediatric health[55-60]. Yet, there has been limited application in asthma[61]. A Cochrane review has shown some benefits of SDM in pediatric asthma, although confidence in findings was rated low-to-moderate because of the lack of suitable controls and high risk of performance and detection bias[62].
A.6. Brief Dyadic SDM Interventions Can be Effective and Scalable. Brief interventions are effective in changing adults' health behaviors[79-84]. Non-asthma caregiver-child dyadic interventions resulted in

children reporting less anxiety[85], less disordered eating[86] and safer driving[87]. Although less is known about brief asthma interventions targeting caregiver-youth dyads, one dyadic intervention was shown to improve caregiver-youth shared asthma management[85]. These data suggest that targeting caregiver-child dyads may amplify, not dilute, intervention effects. Brief interventions (<20 minutes) make up for their brevity by including tailored advice, motivational interviewing (MI)[52] and a plan for follow-up. A directed, patient-centered strategy for eliciting behavior change, MI helps patients explore and resolve ambivalence about recommended health behaviors while not confronting or seeking to change the health beliefs that underlie these behaviors[52]. The synergistic effects of tailoring, SDM, and MI "power" brief interventions in a way that more time- and labor-intensive generic interventions cannot match[79-81]. Since implementation of SDM interventions has been restricted, in part, by burdensome protocols requiring multiple sessions, lengthy engagement and/or time-intensive training for PCPs – protocols ill-suited for FQHCs – we propose to develop **BREATHE-PEDS**, a brief (one-time, 9-minute) SDM intervention that utilizes MI delivered to caregiver-early adolescent dyads by PCPs during office visits for uncontrolled asthma.

A.7. Impact. This study will increase potential access to an asthma intervention for racial/ethnic minority early adolescents, an especially vulnerable group for poor asthma control. The impact of utilizing a brief, one-time FQHC-based intervention and intervening with caregiver-early adolescent dyads could be dramatic.

A.8. Strengths and Weaknesses in the Rigor of Prior Research. The scientific premise for this proposal is strong. Despite high asthma prevalence and morbidity among early adolescents and their unique developmental needs, the field is limited by a lack of developmentally appropriate interventions for this at-risk group. More specifically, most (76%) pediatric SDM interventions exclude children in decision-making[60], even though expert recommendation is that children be involved in health decision-making commensurate with their developmental age and maturity[69,88]. Brief tailored dyadic SDM interventions delivered by PCPs during office visits for asthma directed at fostering evidence-based guideline-directed asthma self-management behaviors (e.g., trigger management, symptom monitoring, medication adherence) has great potential to improve asthma control. Other major limitations of prior research that we improve on include: time-intensive interventions focused on a single aspect of asthma self-management (i.e., medication adherence); intervention visits that occurred outside of clinical care; reliance on highly-trained interventionists; not tailoring interventions; failure to monitor intervention fidelity; lack of an attention control comparator; and a lack of formative process evaluations. We address these limitations and maximize the likelihood of sustaining our intervention and building capacity (scalability) by developing a brief (one-time 9-minute) tailored caregiver-early adolescent dyadic SDM intervention to effect early adolescent's asthma self-management behaviors, using PCPs as interventionists, and implementing rigorous fidelity monitoring protocols (see **C.2.a**) and an attention control group. Integrating self-management SDM discussions into clinical care offers several advantages, such as keeping PCPs more informed regarding their patients' status and health needs, offering them requisite knowledge to improve their asthma self-management. In addition, while prior pediatric SDM interventions often focused only on the caregiver[60,89], intervening simultaneously with caregivers can support the early adolescent's growing autonomy to self-manage asthma[37], and thus asthma control.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

Asthma carries with it some inherent risk (morbidity and, rarely, mortality). Our intervention, however, is educational and behavioral and does not mandate (or prevent) changes in drug therapy or medical management by the study staff. All participants identified as having uncontrolled asthma on screening, regardless of whether they decide to enroll in the trial, will be scheduled for a visit with their PCP who will be notified at the time of screening that their patient's screening indicated uncontrolled asthma. Every attempt will be made to schedule the visit within 14 days of screening; patients will be instructed to seek immediate medical care if their condition deteriorates prior to that visit. While the behavioral

intervention itself is low risk, participants must have uncontrolled asthma to be eligible for enrollment. Because of this, we will ask the Safety Monitoring Board (SMC) to establish a threshold for asthma exacerbations and if we need stop rules, with the team's input.

Because the evaluation utilizes self-reported data, loss of confidentiality of study data is a potential risk. It is also possible that the participants will experience some inconvenience, embarrassment, distress, or fatigue while answering focus group questions/completing surveys. We will allow participants to skip questions and rest as needed.

2.3.2 KNOWN POTENTIAL BENEFITS

Complex behavioral interventions should be informed by stakeholders. Thus, focus group participants will contribute important data that will help us develop a tailored intervention.

The proposed research aims to help early adolescent patients with uncontrolled asthma improve their asthma control thus reducing asthma disparities. Given the minimal risks associated with our behavioral/educational intervention, we believe the benefits outweigh the risks, benefitting the participants. Specifically, those in the **BREATHE-PEDS** group will receive a one-time brief SDM intervention that is expected to improve communication about asthma control and erroneous beliefs, improving symptoms and SDM. Those in the control group may benefit from having a tailored discussion of healthy lifestyles.

We also believe this program will provide benefits to the FQHC personnel. Providers in both the active and control groups will have patients with uncontrolled asthma identified by research staff thereby giving them an enhanced understanding of uncontrolled asthma in their patient population. In addition, those in the **BREATHE-PEDS** arm may learn about erroneous beliefs that are barriers to asthma control and will learn how to deliver a brief behavioral intervention to enhance their patients' motivation to improve disease control.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

Research staff will collect data at the designated time points and the PI will conduct the post-trial interviews. To minimize the risk of inconvenience, embarrassment, distress, or fatigue while completing surveys or interviews, we will allow participants to skip questions and rest as needed. Our team will be trained in all aspects of data collection, procedures for interviewing, and handling sensitive topics in data collection; they will also complete IRB training. Participants can discontinue participation at any time. Weekly team meetings will be used to discuss reactions to the surveys/interviews; we will provide re-training if needed.

3 OBJECTIVES AND ENDPOINTS

Objectives
We propose a feasibility trial to: 1) develop **BREATHE-PEDS** in a pediatric population (dyads of caregivers and their 10- to 14-year-old early adolescents with uncontrolled asthma) receiving asthma care in FQHCs; 2) evaluate the feasibility and acceptability of intervention procedures; and 3) assess intervention effects on asthma outcomes (monthly x 3 months post-intervention).

Endpoint
Primary Outcomes: asthma control as measured by improvements in Asthma Control Questionnaire (ACQ) score.

Secondary outcomes: (a) shared-decision-making as measured by scores the Shared Decision-making Questionnaire – 9 items, (b) Self-management as measured by the Medication Adherence Report Scale – Asthma (MARS-A), (c) asthma and ICS beliefs as measured by the Conventional and Alternative Management for Asthma, (d) asthma quality of life as measured by the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) and Pediatric Asthma Caregiver's Quality of Life Questionnaire; and asthma exacerbations. We will also follow (l) Asthma Impairment and Risk Questionnaire (12 and older) and (m) and Asthma Responsibility Questionnaire scores over time.

Other measures: (1) demographics (age, sex); (2) health literacy as measured by the Newest Vital Sign and the Short Assessment of Health Literacy-English and Spanish.

4 STUDY DESIGN

4.1 OVERALL DESIGN

STUDY DESCRIPTION.
Our overall goal is to develop and test **BREATHE-PEDS (BRief intervention to Evaluate Asthma THErapy-Pediatrics**), a shared decision-making intervention, among low-income urban minority adolescents with uncontrolled asthma.

AIMS. 1) develop **BREATHE-PEDS** in a pediatric population (dyads of caregivers and their 10- to 14-year-old early adolescents with uncontrolled asthma) receiving asthma care in FQHCs; 2) evaluate the feasibility and acceptability of intervention procedures; and 3) assess intervention effects on asthma outcomes (monthly x 3 months post-intervention).

HYPOTHESES.

1. The intervention will be feasible and acceptable as evidenced by: high rates of dyad recruitment and retention; PCP fidelity to the intervention protocol; and PCP and caregiver-child dyad satisfaction.

2. Over 3-months post-intervention, relative to controls, **BREATHE-PEDS** children will have improvement (a) in asthma control as measured by the *Asthma Control Questionnaire*[63-65] (primary outcome), higher perceived SDM, and (b) on other asthma outcomes (secondary outcomes), including quality of life, school absences, lung functioning, and exacerbation.

STUDY PHASE. Phase 1 development and testing a behavioral intervention

STUDY DESIGN. This is a group-randomized clinical trial.

STUDY PROCEDURES.

Aim 1: Focus Groups.
Focus groups. Prior to recruiting for the trial, we will hold focus groups with caregivers (n =20); early adolescents (n =20) and dyads (n =10) (N=60), separately .

Aims 2 & 3: Group-randomized trial. This is a trial of a behavioral/educational intervention comparing the active condition **BREATHE-PEDS (BRief intervention to Evaluate Asthma THErapy-Peds)** to a dose-matched attention control condition (see below for detailed description of conditions). Active and control interventions are delivered once in 9-minutes by the participants' PCP during a single office visit. In each condition there are matched data collection points after baseline: 1-month 2-month, 3-month post-intervention. Considering the potential for visit disruptions due to Covid-19, we offer an alternative plan for the delivery of the intervention at a single telehealth visit (baseline) by phone or HIPAA-compliant videoconferencing platform.

Aim 2: Post-Trial Interviews. The PI will conduct post-trial semi-structured interviews with a purposive sample of ~6 participating clinicians, ~10 patient participants, and ~10 caregivers to ascertain their satisfaction with, and acceptability of, the active and control interventions. As part of our implementation evaluation, attempts will also be made to interview patient participants and PCPs who withdraw from the study (or PCPs who decline to enroll, if we have any), to better understand what it was that prevented their continued participation.

RANDOMIZATION.
We will randomly assign all eligible clinicians equally into the **BREATHE-PEDS** and the dose-matched attention control condition stratified for provider type (physician vs. nurse practitioner [NP]/physician assistant [PA]) using a computer-generated randomization list in advance of the trial. The first four physicians and first four NPs/PAs in each condition (**BREATHE-PEDS** and control) will then be invited to enroll (N=8). Those not selected (i.e., those remaining on the list) will be placed on "standby" if a replacement is needed. Invited PCPs signing consent will then be trained on the condition to which they were randomized. Each PCP will then enroll ~10 dyads meeting inclusion/exclusion criteria (N =85).

STATISTICAL ANALYSES.

Development and Intervention Feasibility. We will document recruitment, randomization and retention success, as well as process and implementation assessments.
Intervention Effects. Intervention effects will be assessed using linear mixed models (LMM) and generalized linear mixed models (GLMM) for continuous and categorical outcomes, respectively[132]. All hypothesis tests will be two-sided at level α=0.05. The key outcome will be ACQ[63-65] score; secondary measures will be examined to inform the future RCT. Separate models will be fitted for different outcome measures. If y_ijt is the outcome for patient j of provider i at time t, without loss generality then the following LMM will be used: $y_{ijt}=\beta_0+\beta_1*Group+\beta_2*t+\beta_3*INT+\beta_4*X_{ij}+\mu_i+\mu_{ij}+\varepsilon_{ijt}$, where group, t, and INT are design variables. Group is an indicator for intervention arm and INT is an indicator for pre- or post-intervention. X_ij is a vector of possible PCP- and patient-level covariates. The random term μ_i iid~$N(0,\sigma_1^2)$ is a PCP-specific random effect and μ_{ij} iid~$N(0,\sigma_2^2)$ is a patient-specific random effect; ε_{ijt} iid~$N(0,\sigma_\varepsilon^2)$ is the model random error. To examine the effect of intervention on the outcome, we will conduct hypothesis test of $H_o:\beta_3=0$. We will explore differential intervention effect by sex (early adolescent and/or caregiver) and conduct exploratory analyses to determine if seasonality or differences in disease severity[108] between groups provide alternative explanations for findings.
Power & Sample Size. With a sample size of 10 dyads/PCP and 4 PCPs in each intervention arm (total n=10*4*2=80), and 20% attrition, we calculated the power to test the effect of intervention on ACQ. Power calculations were based on: (1) 4 repeated observations over the 3-month follow-up with a correlation of ρ=0.8 between repeated measures; (2) intra-cluster correlation among PCPs=0.2 to

account for clustering of patients from the same PCP; and (3) LMMs to estimate pre- and post-intervention differences. We estimated an 80% power to detect a small effect size (d=0.15). For ACQ, this is equivalent to detect a post-intervention difference of 0.15 (assuming SD=0.9).
Qualitative Data. Two or three coders will independently perform conventional content analysis[133]. To enhance rigor, we will use multiple data sources (credibility), rich contextual descriptions (transferability), codebook and saturation tables (dependability) and audit trail (confirmability)[134-137]. NVivo 12 will manage data.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

The control intervention will meet the requirements for a comparison control for testing behavioral interventions[125], which are equivalent in contact time, credible and interesting, and exert limited treatment effects.

5 STUDY POPULATION

Sixty participants (~30 early adolescents with asthma and 30 caregivers of early adolescents with asthma) will take part in pre-trial focus groups. 85 dyads and 8 primary care providers (PCPs) will participate in the trial. Post-trial interview will be conducted We will do post-trial interviews with a purposive sample of ~6 participating clinicians, ~10 patient participants, and ~10 caregivers.

5.1 INCLUSION CRITERIA

Aim 1: Focus groups. Focus group participants will be informal caregivers (e.g., parent, grandparent, older sibling) and children (ages 10-14) with physician-diagnosed asthma. We will conduct focus groups as follows: (a) children aged 10-14 with asthma; (b) caregivers of the children in group a; and (c) dyads who did not participate in group a or b.

Aims 2 & 3: Trial. *Clinician participants* will be eligible if they manage a panel of adult asthma patients. We will enroll eight primary care providers (PCPs) who manage a panel of asthma patients at UHPs two participating sites (4 PCPs / FQHC site). We will enroll 80 children (10- to 14-year-olds) with uncontrolled asthma and their caregivers – 10 dyads per PCP. Based on our prior studies and the data provided to us from the FQHCs, we anticipate 55% of the children aged 10-14 with asthma will be male and 95% will be ethnic-racial minorities (85% Latino; 10% non-Hispanic Black); we anticipate that 95% of the caregivers will be female.

Early adolescent participants: We will enroll early adolescents, informal caregivers and primary care providers. Early adolescents (ages 10-14) will have physician-diagnosed asthma and screen positive for uncontrolled asthma as measured by the Asthma Control Questionnaire. Early adolescent participants must be English-speaking individuals. Caregivers will be informal caregivers (e.g., parent, grandparent, older sibling). Caregivers can be English or Spanish-speaking individuals. Primary care provider participants will be eligible if they manage a panel of pediatric patients.

Aim 2 Post-trial interviews. Post-trial interviews will be conducted with a purposive sample of dyads and PCPs enrolled in the clinical trial.

5.2 EXCLUSION CRITERIA

Exclusion criteria across the study are: 1) serious mental health conditions (caregiver and/or child) or developmental delays (child) that preclude completion of study procedures or confound analyses. Focus group participants will NOT be eligible to participate in the pilot.

5.3 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in this study but are not subsequently assigned to the study intervention or entered in the study. Individuals who do not meet the criteria for participation in this trial (screen failure) because of meeting one or more exclusion criteria that are likely to change over time may be rescreened.

5.4 STRATEGIES FOR RECRUITMENT AND RETENTION

AIM 1: FOCUS GROUPS

Recruitment of participants. We will recruit using three methods.

(1) O*pt-out Letter*: The FQHC administrator/data analyst at each site will create a list of potential participants using a combination of ICD-10 Asthma 493-specific queries of electronic membership records, age, and prescription profile. As in our BREATHE trial, we will employ IRB-approved opt-out letters signed by the federally-qualified health center (FQHC) medical director and mailed to all potential participants. The opt-out letter will identify two active responses and one passive option. The active responses include requesting not to be contacted or calling the research team directly to request screening. The passive response allows the research team to contact the patient if they have not responded within the specified timeframe (i.e., 2 weeks from letter receipt). CU staff will be provided the contact information of eligible patients who were sent letters and did not actively opt out; CU staff and/or UHP staff will then call families to recruit them, explaining the study and collecting consent from those who wish to participate.

(2) *UHP Provider/Staff Referral*: UHP providers and staff will explain the study to eligible dyads who present at the clinic on a given day; they will either consent interested families or refer them to CU staff for consent. UHP may also call their patients; interested patients can be consented orally following the already IRB approved oral script for consenting, or if granted permission to share the caregiver's contact information with CU, pass their information to CU staff who will consent orally using the approved oral consent script.

(3) *Self-referral*: We will also accept participants who respond to recruitment materials. UHP staff will post and/or distribute IRB approved flyers and include the IRB approved slide summarizing the study in their electronic advertising at the clinics; interested patients will contact the CU staff to learn more about the study. Interested families can be consented orally using the approved oral consent script, or in person at the clinic if they have an upcoming appointment.

AIMS 2 & 3: TRIAL

Recruitment of primary care provider (PCPs) participants for pilot trial

Enrolling 8 PCPs participants to the trial. We will recruit 4 primary care providers (PCPs) per site. The clinic will identify PCP participants and trained CU staff will complete a written consent form if done in person or an verbal consent if done orally over the phone. The participating sites have 5 to 14 PCPs who manage a panel of pediatric asthma patients.

Enrollment feasibility

We will enroll 30 dyads (caregiver-child) for focus groups and 85 dyads for the trial (trial dyads cannot have participated in focus groups).

Aim 1: Focus Groups: Participants will be informal caregivers (e.g., parent, grandparent, older sibling) and children (ages 10-14) with physician-diagnosed asthma.

Aims 2 & 3 Clinical Trial – Dyads: We will enroll early adolescents, informal caregivers and primary care providers. Early adolescents (ages 10-14) will have physician-diagnosed asthma (and screen positive for uncontrolled asthma as measured by the Asthma Control Questionnaire. Caregivers will be informal caregivers (e.g. parent, grandparent, older sibling). Primary care provider participants will be eligible if they manage a panel of pediatric patients.

Data provided by Urban Health Plan Inc. indicates that they follow a panel of 1,896 children aged 10-14 with asthma who are prescribed controller in the past year; of these 596 have uncontrolled asthma as indicated by an asthma control test score administered at their last appointment. Considering our 60% success rate for enrolling dyads in our previous trial, this would yield 358 dyads for enrollment (we need only 30 dyads for focus groups and 40 dyads for the trial).

Aims 2 & 3 Clinical Trial – PCPs: Based on the strong FQHC support for this project and the fact that in our pilot BREATHE study, all PCPs approached agreed to participate, we do not anticipate difficulty in recruiting PCPs. Moreover, we will replace a PCP should a PCP decline to enroll or drops out before end of study; we have a sufficiently large waitlist of PCPs (and additional sites) from which to replace PCPs, if needed.

Vulnerable Subjects

Asthma's impact is significant among minority populations. Erroneous beliefs impede asthma control. To date, community-based asthma interventions have not reduced the burden of asthma. For this reason, we adapted an evidence based brief SDM intervention used in acute care settings to FQHC settings with input from black adult asthma patients and their loved ones. We will develop this intervention by adapting our prior work in our adults which found several positive short-term effects on asthma control, SDM, and symptom burden.

Pregnant women will be eligible to participate since improving asthma control for their early adolescent children would benefit the family.

Retention of patient participants

UHP has retained 72-90% of participants in clinical trials requiring data collection of 12 months (Personal communication, F. Barsanti). To retain 80% of dyads over 3 months post-intervention for this trial, we will use the retention strategies proven successful in our previous trials in FQHCs requiring 3+-months of follow-up:

1. Assigning one Research Assistant (RA) to a dyad: Data collection by RAs that have a history of working at these FQHCs will facilitate rapport and retention. RAs are often members of the community; all have received training on the delivery of patient-centered care.

2. Confirming contact information at each assessment; obtaining contact information of two or more people who will know how to contact the participant: We will update contact information (e.g., name, address, phone numbers, emails) for the participants and two or more of their contacts at each study visit; participants will be asked to indicate preferred mode of communication (email, text or phone).

3. Frequent data collection points: There are 4 assessment points over the 3-month follow-up. Participants will receive monthly communication from our study team to confirm upcoming visits. If they fail to respond after three attempts using multiple modes of contact over varying day/evening hours and weekday/weekend attempts, we will contact their alternative contacts.

4. Graduated incentives: Participants will be compensated using a graduated incentive plan. We will pay the dyad: baseline=$25; 1-month=$30; 2-month=$40; 3-month=$50 (total $145). A portion of each incentive will be made directly to the child**.**

Retention of PCP participants

Since we have FQHC administrative buy-out of PCP time and strong support for this project and because each PCP delivers the intervention only one-time to small number of their patients , we do not anticipate difficulty with PCP retention. We will replace a PCP should a PCP drop out and we have a sufficiently large waitlist of PCPs (and additional sites) from which to choose, if needed.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

DESCRIPTION OF STUDY INTERVENTIONS.

BREATHE-PEDS Intervention. BREATHE, grounded in shared decision-making (SDM) theory and developed with input from black adults with asthma, utilizes PCPs to deliver a brief intervention using motivational interviewing in a single brief (9-minute) intervention during an office visit. Using data we collect from our focus groups we will develop **BREATHE-Peds** by adapting BREATHE. PCPs follow a 4-step script developed in partnership with patients and tailored to specific erroneous beliefs measured by the Conventional and Alternatives Management for Asthma (CAM-A) survey, as well as to their Asthma Control Questionnaire (ACQ) score. A lab coat pocket-sized laminated action card will supplement the

web-based application that the PCPs follow prompting them through the intervention. The tailored script is automatically generated based on the RA inputting the CAM-A and ACQ responses. We will randomize providers to one of two intervention arms. Neither intervention alters the clinical care study participants receive. Our intervention involves training providers on communication methods/topics; it does not involve our changing or modifying patient medication in any way. Patients in both arms receive the same asthma care from the providers.

- Step 1: Raise the subject (1½ minute). PCP establishes rapport using persuasive communication techniques and assesses the dyad's asthma knowledge, perception of asthma control, quality of life, self-care preferences, and motivation for enhanced asthma control, exploring specific asthma and ICS beliefs that they have endorsed and that are known to be associated with uncontrolled asthma.
- Step 2: Provide feedback (1½ minutes)**.** PCP provides feedback to the dyad based on assessments made in the prior step. The PCP candidly discusses the patient's uncontrolled asthma and erroneous beliefs in the context of gaps in asthma self-management, drawing a connection between current self-management and uncontrolled asthma.
- Step 3. Enhance engagement (3 minutes). The PCP attempts to enhance the dyad's motivation to increase Self-management using motivational interviewing techniques such as collaboration, empathy, concern, and acceptance of ambivalence about self-care. In this step, the PCP may elicit the dyad's beliefs regarding the benefits, and negative sequelae, of their current degree of self-management (pro/con).
- Step 4: Shared decision-making (3 minutes). The PCP and dyad jointly consider treatment options. The PCP will actively attempt to build consensus around self-management, reconciling conflicts to better align asthma and ICS beliefs with evidence-based guideline-directed treatment. For example, if the patient uses ICS intermittently (rather than twice daily as required) because of an erroneous belief that tolerance to ICS develops with daily dosing, then the PCP will attempt to counter that belief using the tailored script, as well as information from national asthma guidelines. This will likely include encouraging the patient to use ICS once a day (50% adherence) as an initial short-term plan to be followed by a return visit and re-evaluation of asthma control. If the patient declines to engage in SDM or declines attempts at negotiating ICS use, then the PCP and the patient agree to disagree.

Dose-matched Attention Control Intervention. The control intervention will meet the requirements for a comparison control for testing behavioral interventions, which are equivalent in contact time, credible and interesting, and exert limited treatment effects. Control participants will receive a PCP-led 9-minute scripted discussion tailored to healthy lifestyles (e.g., diet, exercise) following Teach to Goal principles:

- Review of weight, diet and exercise: (3 minutes). PCP and patient review current weight/fitness, current diet and/or current exercise in the context of goal-setting.
- Exercise counseling: (3 minutes). PCP describes benefits of exercise and options for starting/increasing exercise.
- Plan for goal attainment (3 minutes)**.** PCP explores barriers and facilitators to goal attainment.

Control PCPs will use study the web-based app to access the healthy lifestyle scripts and patient participant's ACQ score but will not have access to CAM-A results or **BREATHE-PEDS** scripts. While control participants will receive important nutrition and lifestyle information, the control intervention is not designed to be specific enough to change strategies related to ICS adherence. Further, the control group offers a similar format as BREATHE-PEDS, namely PCP-led discussions in which PCPs use tablets to review ACQ scores and initiate a tailored discussion.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

Intervention Training, Supervision and Fidelity. We have extensive experience training clinicians to deliver interventions, as well as monitoring treatment fidelity. Procedures used in this study will mirror established procedures employed in our BREATHE-PEDS pilot.

- BREATHE-PEDS Training. The core training for PCPs delivering the **BREATHE-PEDS** intervention will be conducted by our consultant, Dr. Pantalon, and will consist of one, 2-hour instructional session comprised of: didactics - 30 minutes; role-playing common clinical scenarios - 10 minutes; SDM role-playing - 50 minutes; question & answers – 30 minutes. Immediately after training, PCPs will be tested using a standardized patient scenario to demonstrate that he/she can deliver the intervention in 9 minutes or less, the average length obtained in our feasibility trial. If the PCP fails to achieve 100% proficiency, she/he will receive additional instruction and retested. Prior studies demonstrated that remediation re-training results in 100% proficiency.
- Attention Control Training. PCPs assigned to the attention control condition will be trained using a 15-minute self-guided instructional manual followed by an in-person question and answer period with the PI.
- Supervision and fidelity. We will audio record all participants' intervention) visits (**BREATHE-PEDS** and control). The Research Assistant (RA) will set up two digital recorders at the beginning of the visit and upload audio files to a secure HIPAA-compliant site within 24 hours of the visit. Within 24 hours of recording, files will be uploaded and 2-3 trained raters, working independently of one another, will review the sessions. We will evaluate fidelity the first time a PCP delivers their intervention and then at ~20% of randomly selected visits, a protocol successfully used by the consultant. At least one additional file per PCP will be reviewed prior to enrollment of their 5th participant, to evaluate drift and the length of sessions. For **BREATHE-PEDS** we will determine whether the critical elements of the brief intervention were completed in 9 minutes using the validated Brief Negotiation Interventions Adherence Scale adapted to asthma. For the control sessions, raters will note the length and content of the healthy lifestyle discussion. Within 24 hours of the rating, the PCPs will receive a summary of their performance (free of personal health identifiers) via email. PCPs will receive additional training to enhance intervention fidelity and dose (length) if problems are identified (by Dr. Pantalon for **BREATHE-PEDS** group and Dr. George for control group). PCPs will not be excluded from the study if they fail to deliver all elements of their respective intervention. PCPs will not be excluded if they require more (or less) than 9 minutes to deliver the intervention. Control PCPs will not be excluded if they teach asthma self-care; these metrics will be tracked.

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

DESCRIPTION OF RANDOMIZATION PROCEDURES: Prior to trial initiation, all eligible clinicians will be randomized equally into the BREATHE and the attention control condition stratified for provider type, using a computer-generated randomization list. We will obtain informed consent from the first eight clinicians on the randomization list: four/site; two physicians and two nurse practitioners [NPs]

randomized to BREATHE; two physicians and two NPs randomized to control. Those remaining on the list will be placed on "standby" if replacement is needed.

CONTAMINATION.
Contamination will be minimized by (1) training only **BREATHE-PEDS** clinicians to deliver the active intervention and (2) encouraging confidentiality regarding training and intervention content.

MASKING.
Dyads, data collectors, and the statistician will be blinded to assignment. Consent materials will inform dyads that the focus of the trial is on the communication they have with their clinician about asthma management and control. Immediately after the intervention, dyads will be asked to guess the condition to which their clinician had been randomized. At the end of participants' final data collection visit, data collectors will be asked to guess whether participants had received the active or control intervention at the visit. These data will provide some measurement of the success of masking.

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

Stop rules. If the PI, IRB and/or SMC determines that stop rules are warranted for serious adverse events then data collection and study enrollment will be stopped. The SMC and the IRB will be asked to review the study and suggest modifications of the protocol, the threshold limit or other changes. If the SMC and the Chairperson of the IRB believe that these modifications are adequate for resumption of the study, then the study will resume. NINR will receive a written report within three days of any such suspension and/or resumption of data collection.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are free to withdraw from participation in the study at any time upon request.

7.3 LOST TO FOLLOW-UP

A participant will be considered lost to follow-up if he or she fails to return for TBD number of scheduled visits and study staff are unable to contact the participant after more than 3 attempts.

The following actions must be taken if a participant fails to return for a required study visit:

- The site will attempt to contact the participant, reschedule the missed visit, counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study

- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts will be documented in the participant's medical record or study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES

Caregivers and children will complete assessments at four timepoints: baseline, immediately after the medical visit, and 1-, 2-, and 3-months following the child's asthma visit. The baseline and 1

The measures completed at each time point by each participant are detailed in the table below as well as in the endpoints section on pages 3-5.

MEASURE	TIMEPOINT						COMPLETED BY		
	Screening	Base	Immed	1-Mon	2-Mon	3-Mon	Caregiver	Child	Clinician
Asthma Control Questionnaire	X	X		X	X	X	X	X	
Shared-Decision-Making Questionnaire			X				X	X	X
Medication Adherence Record Scale-Asthma		X		X	X	X	X	X	
Conventional & Alternative Management for Asthma	X	X		X	X	X	X	X	
Pediatric Asthma Quality of Life Questionnaire		X		X		X		X	
Pediatric Asthma Caregiver's Quality of Life Questionnaire		X		X		X	X		
Asthma Impairment & Risk Questionnaire (AIRQ)		X		X	X	X		X (>12-years-old)	
Brief debriefing survey			X				X	X	X

Asthma exacerbation				X	X	X	X		
Asthma Responsibility Questionnaire		X		X	X	X		X	
Newest Vital Sign		X					X		
Short Assessment of Health Literacy		X					X		
Asthma Prevention Index		X		X	X	X	X	X	
Asthma history & demographics		X					X	X	

8.1 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.1.1 DEFINITION OF ADVERSE EVENTS

Adverse events are defined as unanticipated problems involving risks to study participants or others, or as any untoward medical occurrence that may present itself during the study time period which may or may not have a causal relationship with the treatment.

8.1.2 DEFINITION OF SERIOUS ADVERSE EVENTS

Serious adverse events result in any of the following outcomes: death, a life-threatening experience, inpatient hospitalization, or a significant disability/incapacity. Such events also include breeches of confidentiality.

8.1.3 CLASSIFICATION OF AN ADVERSE EVENT

8.1.3.1 SEVERITY OF EVENT

All AEs should be assessed by the principal investigator, and if necessary, another professional with clinical
Moderate adverse events are those discomforts severe enough to cause interference with usual activities or requiring treatment by a health care provider. Such events also include the loss of participants from the study for reasons related in any way to a deviation from procedures for ensuring confidentiality.

Mild adverse events are those events that are easily tolerated signs or symptoms of discomfort; minor irritants that cause no loss of time from normal activities; symptoms that require no medication or a medical evaluation; and transient signs and symptoms.

8.1.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

The SMC will then determine how an AE is to be categorized using standard taxonomy: Unrelated (clearly not related to the research), Unlikely (doubtfully related to the research), Possible (may be related to the research), Probable (likely related to the research) and Definite (clearly related to the research).

8.1.3.3 EXPECTEDNESS

Unexpected adverse events are those events, the specificity or severity of which is not consistent with the risk information described in the general investigative plan or the IRB proposal. "Unexpected" refers to an adverse event that has not been previously observed.

Expected adverse events are those events, the specificity or severity of which is consistent with the risk information described in the general investigative plan or IRB proposal.
Any ED visit or hospitalization associated with primary ICD-10-CM Diagnosis Code 493. Asthma (493.00 asthma atopic unspecified; 493.01 asthma atopic asthmaticus; 493.02 asthma atopic acute exacerbation; 493.10 intrinsic asthma unspecified; 493.11 intrinsic asthma asthmaticus; 493.12 intrinsic asthma acute exacerbation; 493.20 asthma chronic obstructive pulmonary disease copd; 493.21 asthma chronic obstructive pulmonary disease copd; 493.22 asthma chronic obstructive pulmonary disease copd; 493.81 exercise induced bronchospasm; 493.82 cough variant asthma; 493.91 asthma bronchial allergic nos asthmaticus; 493.92 asthma bronchial allergic nos acute exacerbation) will be characterized as a Probable or Definite SAE.

8.1.4 ADVERSE EVENT REPORTING

AEs and SAEs will be systematically assessed at all data collection points via review of the medical record and/or patient interview. Subjects will be instructed to report AEs and SAEs to the study team within 48 hours of their occurrence.

During the trial, subjects will be instructed to notify the study team within 48 hours of any Emergency Department (ED) visit or hospitalization, regardless of its cause, and to notify the study team within 48 hours of initiating oral corticosteroids (OCS), each event representing the standard definition of asthma exacerbation. Because not all exacerbations cause individuals to seek acute care, we will track OCS use and intensification of beta-agonist use as those who manage an exacerbation outside of the ED or hospital will manage their exacerbation in this manner. We will also ask subjects to report these at monthly data collection points in an attempt to capture any exacerbations that might otherwise go unreported. In this manner we will not miss any exacerbations. Subjects' answers will then be compared to the medical record and/or claims data, as available.

8.1.5 SERIOUS ADVERSE EVENT REPORTING

SAE reporting.

Any SAE whether related to study intervention, will be reported to the IRB and the SMC. The PI will inform the IRB and SMC immediately and jointly decide whether the reported event is a SAE that must be reported to NINR due to the unexpectedness and/or the severity of the event. If it is determined that it is either unexpected and/or the severity, the SAE will be reported to NINR within two days.

In the event that a patient either withdraws from the study or the investigator decides to discontinue a patient due to SAE, the patient will be monitored by the investigator via ongoing status assessment until 1) a resolution is reached, i.e., the problem requiring hospitalization has resolved or stabilized with no further changes expected; 2) the SAE is determined to be clearly unrelated to the study intervention; or 3) the SAE results in death. A summary of the SAEs that occurred during the previous year will be included in the annual progress report to the IRB and the SMC. The report will include the participants' sociodemographic characteristics, expected versus actual recruitment rates, treatment retention rates, any quality assurance or regulatory issues that occurred during the past year, summary of AEs and SAEs, and any actions or changes with respect to the protocol.

8.2 UNANTICIPATED PROBLEMS

8.2.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.]

8.2.2 UNANTICIPATED PROBLEMS REPORTING

The investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB) and to the DSMP/lead principal investigator (PI). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP.

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Specific Aims:

1. To develop **BREATHE-Peds** in a pediatric population (dyads of caregivers and their 10- to 14-year-old early adolescents with uncontrolled asthma) receiving asthma care in FQHCs;

2. To evaluate the feasibility and acceptability of intervention procedures; and

3. To assess intervention effects on asthma outcomes (monthly x 3 months post-intervention).

Hypotheses:

1. The intervention will be feasible and acceptable as evidenced by: high rates of dyad recruitment and retention; PCP fidelity to the intervention protocol; and PCP and caregiver-child dyad satisfaction.

2. Over 3-months post-intervention, relative to controls, **BREATHE-Peds** children will have improvement (a) in asthma control as measured by the Asthma Control Questionnaire (primary outcome), higher perceived SDM, and (b) on other asthma outcomes (secondary outcomes), including quality of life, school absences, lung functioning, and exacerbation.

MEASURES / ENDPOINTS.

Primary Outcomes: asthma control as measured by improvements in Asthma Control Questionnaire (ACQ) score.

Secondary outcomes: (a) shared-decision-making as measured by scores the Shared Decision-making Questionnaire – 9 items, (b) Self-management as measured by the Medication Adherence Report Scale – Asthma (MARS-A), (c) asthma and ICS beliefs as measured by the Conventional and Alternative Management for Asthma, (d) asthma quality of life as measured by the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) and Pediatric Asthma Caregiver's Quality of Life Questionnaire; and significantly lower rates of (e) asthma exacerbations, (f) symptoms days, (g) nights woken, (h) activity limitations, (i) shortness of breath, (j) wheeze, and (k) rescue medicine use. We will also track Asthma Impairment and Risk questionnaire and Asthma Responsibility Questionnaire scores over time.

Other measures: (1) demographics (age, sex); (2) health literacy as measured by the Newest Vital Sign and the Short Assessment of Health Literacy-English and Spanish; (3) asthma history and (4) lung function as measured by spirometry (COVID permitting).

9.2 SAMPLE SIZE DETERMINATION

Power & Sample Size. With a sample size of 10 patients/PCP and 4 PCPs in each intervention arm (total n=10*4*2=80), and 20% attrition, we calculated the power to test the effect of intervention on outcomes. Power calculations were based on: (1) 4 repeated observations over the 3-month follow-up with a correlation of ρ=0.8 between repeated measures; (2) intra-cluster correlation among PCPs=0.2 to account for clustering of patients from the same PCP; and (3) LMMs to estimate pre- and post-intervention differences. We estimated an 80% power to detect a small effect size (d=0.15). For ACQ, this is equivalent to detect a post-intervention difference of 0.15 (assuming SD=0.9).

9.3 POPULATIONS FOR ANALYSES

INTENTION-TO-TREAT (ITT) ANALYSIS POPULATION (i.e., all randomized participants)

QUALITATIVE ANALYSIS AND RIGOR. Analysis of Qualitative Data. Guided by Qualitative Descriptive methodologies, 2-3 coders working independently of each other will systematically read the focus group transcripts to identify codes and categories using conventional inductive content analysis. An iterative codebook will be developed, and a data saturation table will be created and maintained in tandem with updates to the codebook. Data saturation, a measure of data adequacy, will signal the end of data collection (focus groups) and analysis. The creation of saturation data tables adds transparency to the process. Saturation can be reached with a small number of focus groups when the scope of the project is narrow and there is sample homogeneity (e.g., minority dyads from the same community), as in this proposal.

Directed content analysis will be used to summarize satisfaction at post-trial interviews using constructs from the Theoretical Framework of Acceptability (e.g., burden, user experience, attitudes towards the intervention and intention to participate).

Various methods of enhancing the rigor of qualitative methods will be used. Credibility will be enhanced by having disagreements about codes reconciled by consensus and by returning our findings to a small group of participants who will perform a "member check" to determine if the categories resonate with them. We will also use triangulation, a method in which multiple data sources (e.g., dyads, primary care providers) describe their perspectives. Investigators with disparate expertise (e.g., nurse scientists, public health and behavioral scientists) will serve as coders and have collaborated on the design of the trial, providing additional triangulation. Our purposive sample fosters transferability, the ability to translate findings to similar communities. Dependability and confirmability criteria will be met by the creation of an audit trail documenting data collection and analysis decisions. NVivo 12 will be used to manage qualitative data

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

Participants will be described with respect to baseline characteristics (e.g., means, standard deviations, ranges, etc.) Descriptive data analysis will precede formal hypothesis testing to understand the data distribution and to check for outliers to determine the need for transformations of variables or special analytic techniques. We will also examine the patterns of missing data paying special attention to the balance of missing data in the study arms; linear and generalized linear mixed models provide unbiased estimates for data with missing at random when likelihood of missing is not related to the missing data and can be fully accounted for by variables where there is complete information. Intention-to-treat analyses will be conducted which requires data to be analyzed as randomized, regardless of whether participants completed some or none of the intervention. Based on our feasibility trial and the high retention rate in our previous trials, we anticipate 90% will provide baseline, 1-, 2-, and 3-month data.

9.4.2 ANALYSIS OF THE PRIMARY AND SECONDARY ENDPOINT(S)

Analytic Plan.

Aims 1 & 2: Development and Intervention Feasibility. We will document our success in meeting recruitment and randomization goals, as well as process (recruitment outreach and numbers meeting eligibility criteria who accept or decline enrollment) and implementation assessments (retention rates, data completion rates, as well as fidelity, contamination and masking in the clinical trial arm).

Randomization. This is a group-randomized trial in which the primary care providers (PCPs) will be randomized within sites to the active and control conditions. We will utilize a stratified block randomization plan, stratifying by provider type (physician vs. nurse practitioner/physician assistant), to insure equal numbers of PCPs within each PCP type are assigned to each condition. Randomization lists will be computer-generated in advance by our biostatistician. Outcomes will be analyzed at the level of the early adolescent and/or caregiver.

Masking. Participants and data collectors will be masked to study hypotheses and group assignment; the investigators will be blinded to group assignment. PCPs in both intervention conditions will use tablets as part of their respective interventions and have sessions audio-recorded, facilitating masking of participants and data collectors.

Aim 3: Intervention Effects. Intervention effects will be assessed using linear mixed models (LMM) or generalized linear mixed models (GLMM) for continuous and categorical outcomes, respectively. All hypothesis tests will be two-sided at level $\alpha=0.05$. The key outcome will be ACQ score; secondary measures will be examined to inform the future RCT. Separate models will be fitted for different outcome measures. If y_{ijt} is the outcome for patient j of provider i at time t, without loss generality then the following LMM will be used:
$y_{ijt}=\beta_0+\beta_1*Group+\beta_2*t+\beta_3*INT+\beta_4*X_{ij}+\mu_i+\mu_{ij}+\varepsilon_{ijt}$, where group, t, and INT are design variables. Group is an indicator for intervention arm and INT is an indicator for pre- or post-intervention. X_{ij} is a vector of possible PCP- and patient-level covariates. The random term μ_i $iid\sim N(0,\sigma_1^2)$ is a PCP-specific random effect and μ_{ij} $iid\sim N(0,\sigma_2^2)$ is a patient-specific random effect; ε_{ijt} $iid\sim N(0,\sigma_\varepsilon^2)$ is the model random error. To examine the effect of intervention on the outcome, we will conduct hypothesis test of $H_o:\beta_3=0$. We will explore differential intervention effect by sex.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms will describe in detail the study intervention, study procedures, and risks and documentation of informed consent will be completed prior to starting the study intervention. These

forms include: adult (caregiver) consent for their own participation and their child's participation, and adolescent assent for participation.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

The informed consent process includes reading the informed consent to the dyad and answering questions. Oral explanations provided to both children and caregivers will convey who is conducting the study, the purpose of the study, the procedures (e.g., the number of surveys), study risks and benefits, a discussion of compensation, and a statement that participation is voluntary; all oral explanations and written consent/assent forms will be IRB and HIPAA compliant. Those who remain interested after review of the consent/assent form and after questions have been answered will be asked to sign the consent/assent form.

Consent will be obtained several ways, which correspond to the methods of recruiting.

(1) Opt-Out Letter: Following the two-week period allocated to allow participants to actively opt out, CU and/or UHP staff will contact eligible families by phone who have if not opted out. We explain the study to them providing all the details needed for families to make an informed decision to participate and will obtain their oral consent and assent if they wish to participate using the already approved IRB oral script for consenting. We will document oral consent in study logs, including the date/time of consent/assent, the name of the caregiver and adolescent, and the staff member collecting the consent/assent.

(2) UHP Provider/Staff Referral: UHP providers and staff will explain the study to patients who present at the clinic on a given day; they will either obtain written consent from interested families using our IRB approved consent forms. Or they may refer them to CU staff for consent. If CU staff are at the clinic, they will explain the study to patients in person and obtain written consent. Otherwise, they will call the family and obtain oral consent as detailed in recruiting option #1 above. UHP staff may also call eligible patients to explain the study to them and if interested consent them orally.

(3) Self-referral: We will also accept participants who respond to recruitment materials, such as posted flyers and the slide that is part of UHPs electronic messaging. Interested patients will contact the CU staff to learn more about the study. CU staff or UHP staff will consent the family in person when possible and obtain written consent; otherwise consent will be obtained via phone and oral consent/assent will be obtained as detailed in #1.

The consent form includes HIPAA authorization. Copies of signed consent form will be secured in electronic form behind the Columbia firewall or in hardcopy in a locked cabinet in a locked office at CUSON. Trained research assistants will answer questions in the same manner as if the consent was being obtained in-person.

COVID-19 CONSIDERATIONS. If social distancing mandates prevent us from obtaining informed consent or study visits/procedures in-person, we will follow an IRB-approved script to obtain oral consent using telephone or secure web-based videoconferencing platform that is HIPAA-compliant, documenting name, date and time of oral consent.

PHASE 2 only. We will use the same IRB approved screening protocol from our prior trials that allowed us to obtain screening data by phone (asthma control score) with an initial verbal consent from the caregiver

and child assent. Those children whose asthma control score indicates that they have uncontrolled asthma will have their baseline visit scheduled within ~14 days. If at any time the children experience a loss of asthma control, they will be told to seek immediate medical attention. Written consent/assent will be obtained as previously described.

10.1.2 CONFIDENTIALITY AND PRIVACY

We will ensure confidentiality is protected by taking several steps. All members of the study staff complete training in human participants' protection, HIPAA requirements, as well as ongoing training by the PI and the investigators in all aspects of human subject protection. The formal training program will include a course on Good Clinical Practices. For purposes of the research database, individuals seen at participating sites will be assigned a unique identifier that bears no systematic relation to their health records. Information to be excluded from the research database includes names of study participants (and their contacts), as well as addresses, telephone numbers, FQHC, clinician(s), and other information that has the potential to identify individuals. Data managers and the research staff will be responsible for data management of the information collected and will be supervised by the MPIs George & Bruzzese. Data will be stored on a password-protected webserver, which Columbia University staff can access for data entry; files stored on the webserver are also encrypted. All research participants will be identified on all research forms and logs other than consent forms by coded identifiers. Codebooks relating ID codes to names will be personally maintained only by Dr. George in a locked cabinet and/or in an electronic file that is password-protected and stored behind the Columbia firewall. Confidentiality of all participants will be optimized by housing all paper records in locked files in locked offices. Electronic data will be maintained on a computer in password-protected computer files with limited access to data by staff – different levels of access will depend on the person's specific level on the staff, and server security safeguards that in the aggregate provide a high degree of protection from unauthorized users. All the information will be coded by identification number so that no names are associated with any of the data. The identity of participants will not be revealed in the presentation or publication 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.

10.1.3 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored, with the participant's approval and as approved by local Institutional Review Board (IRB). No specimens will be collected.

10.1.4 SAFETY OVERSIGHT

DATA SAFETY AND MONITORING PLAN (DSMP)

Institutional Review Board (IRB) Oversight

The Columbia University Human Research Protection Office (HRPO) and Institutional Review Board (IRB) has determined that Columbia University IRB will serve as the single Reviewing IRB for this research. This is designated in the application and in accordance with the Department Health and Human Services regulation for the use of a single IRB for federally funded collaborative research under the Revised Common Rule. The applicant organization (Columbia University) and Multiple Principal Investigators (MPIs) (George [contact PI] and Bruzzese) are responsible for overseeing all research activities and

remaining compliant with applicable regulations, grant requirements, and the terms of the IRB approval. The DSMP will be reviewed and approved by the IRB prior to any human participants' research and renewed annually.

Data and Safety Monitoring Board (DSMB)/Safety Monitoring Committee (SMC)

At the initiation of this study, we will create a three-member DSMB/SMC of persons not affiliated with the research project, which will include one person outside of the institution, one person with statistical expertise, and one person with medical expertise in adolescent asthma. Names were submitted to the NINR and approved on October 18, 2021. The approved SMC are:

Chair Jonathan Feldman PhD. Clinical Associate Professor, Department of Pediatrics, Albert Einstein College of Medicine & Professor of Psychology, Ferkauf Graduate School of Psychology Yeshiva University. jonathan.feldman@yu.edu Dr. Feldman has a federally funded program of research using behavioral interventions to improve asthma symptom perception and medication adherence in children and adults with asthma; psychological treatment of anxiety in patients with asthma; anxiety, depression, and food allergy.

Member Shing Lee, PhD. Associate Professor Biostatistics at the Columbia University Medical Center. sml2114@cumc.columbia.edu Dr. Lee's research interest is in the implementation of novel designs for early stage trials. Lee has over ten years of experience in statistical consulting. She has assisted numerous investigators from a variety of medical disciplines in the design, conduct and analysis of clinical studies.

Member Tina Tolomeo, DNP, MBA, APRN, FNP-BC, AE-C. Senior Director, Patient Access Yale Medicine and Nurse Practitioner in the Department of Pediatrics. Tina joined the Section of Pediatric Respiratory Medicine at Yale in 1995. Her academic and clinical interests include, but are not limited to, asthma, general pediatric pulmonary medicine, patient access, and patient self-management.

The approved DSMB/SMC members will review and finalize the DSMP that the MPIs draft. The finalized DSMP will be sent to the IRBs and the NINR Program officer prior to the onset of study enrollment.

The purpose of the DSMB/SMC is to protect participant safety and to monitor study performance and the quality and integrity of all study-related activities. As such, the DSMB/SMC will review informed consent/assent procedures, any modifications to the study protocol, and all adverse events (AEs). The DSMB/SMC will be privy to statistical data and case reports required for its deliberations. The DSMB/SMC will meet twice per year by phone/videoconferencing and more if needed. Official minutes will be taken and will be available to NINR after upon request.

The DSMB/SMC will provide recommendations to the MPIs about starting, continuing, altering, and completing each of the studies. In addition, the DSMB/SMC will:

- Review and finalize the Data Safety Monitoring Board/ Safety Monitoring Committee Charter;
- Review informed consent/assent procedures, protocols, and any modifications to protocols, and all AE reporting forms and procedures prior to initiating any of the studies;
- Approve the definition of AEs, including serious adverse events (SAE); and
- Review and finalize the plan for reporting AEs to organizations with oversight responsibilities.

The purpose of the DSMB/SMC is to protect participant safety and monitor study performance and the quality and integrity of all study-related activities. As such, the DSMB/SMC will review informed consent

procedures, any modifications to the study protocol, and all AEs. The DSMB/SMC will define AEs, which are expected to include oral steroid bursts, excessive rescue medicine use, Emergency Department (ED) visits and hospitalizations, as well as SAEs, which are expected to include any life-threatening exacerbations, admissions to ICU, events that result in permanent disability, or deaths. AEs and SAEs can be related to the study intervention or not and can be expected or unexpected. The DSMB/SMC will also establish a plan for reporting AEs to agencies. All staff will be instructed to report any AE or problems involving risk to the MPIs. The MPIs or Dr. Kattan, our pediatric pulmonologist co-investigator, will review the AE with the participant, and in compliance with the plan, the MPIs will report AEs to appropriate agencies. Based on the Safety Monitoring Committee and DSMPs in our prior studies, we anticipate deaths and formal study complaints will be reported in real time to the DSMB/SMC, IRBs, and NINR if study-related; other SAEs are reported bi-annually. The NIH Program Officer will also be informed if action is taken by the DSMB/SMC or IRB. The DSMB/SMC will also define thresholds for participant safety, rules for stopping protocols, and nature/frequency of reports for its review. The DSMB/SMC could stop the trial if there were a disproportionate number of ED visits or hospitalizations, oral corticosteroids (OCS) bursts, or excessive intensification of rescue medication use attributed to study participation.

Data and Safety Monitoring Procedures

The MPIs will be responsible for ensuring that any risks to study participants are minimized. In their weekly team meetings, the MPIs and the Co-Investigators will review data reports regarding all study-related activities. This will include screening, consent/assent, intervention activities, and surveys/interviews. Because this study involves testing a behavioral intervention and does not involve dispensing medication, it does not pose a serious health risk to study participants. Despite this, all study personnel will report any study-related AEs and/or unanticipated problems (UPs) involving risks to participants to the MPIs. After a prompt, careful review of the events, the MPIs will report the event to the IRBs and the DSMB/SMC if deemed necessary. The contact PI (George) will also inform her NINR Program officer in writing of any actions taken by the IRBs because of such AEs, cc'ing Dr. Bruzzese.

While we anticipate the intervention will improve asthma control and reduce asthma morbidity, it is possible that study participants have more AEs than controls because of an increased awareness of the role of their suboptimal self-management in uncontrolled asthma. Therefore, the DSMB/SMC will also monitor for reverse effects.

During the trial, participants will be instructed to notify the study team within 48 hours of any ED visit or hospitalization, regardless of its cause, and to notify the study team within 48 hours of initiating OCS or excessive intensification of rescue medication (to be defined by the DSMB/SMC), each event representing the standard definition of asthma exacerbation. We will also ask participants to report these events within 48 hours of their occurrence, but we will also query about these events at each data collection point to capture any exacerbations that might otherwise go unreported. Participants' answers will then be compared to the medical record and/or claims data, as available. Exacerbation rates more than the threshold set by the DSMB/SMC may trigger an immediate study shutdown.

The DSMB/SMC will determine how an AE is to be categorized using standard taxonomy: Unrelated (clearly not related to the research), Unlikely (doubtfully related to the research), Possible (may be related to the research), Probable (likely related to the research) and Definite (clearly related to the research). They will also address Unanticipated Problems (UP). In this study we will also use the FDA definition of a SAE: deaths, hospitalization, toxicity, all life threatening or disabling/incapacitating events, and all congenital abnormalities or birth defects among research participants.

UPs, AEs, & SAEs

The DSMB/SMC will adhere to the Office of Human Research Protections (OHRP) definitions for AEs, SAEs, and UPs using the following OHRP definitions:

AEs are defined as UPs involving risks to study participants or others, or as any untoward medical occurrence that may present itself during the study period which may or may not have a causal relationship with the treatment. Such events may also include breaches of confidentiality.
SAEs result in any of the following outcomes: death, a life-threatening experience, inpatient hospitalization, or a significant disability/incapacity.
Moderate AEs are those discomforts severe enough to cause interference with usual activities or requiring treatment by a health care provider. Such events also include the loss of participants from the study for reasons related in any way to a deviation from procedures for ensuring confidentiality.
Mild AEs are those events that are easily tolerated signs or symptoms of discomfort; minor irritants that cause no loss of time from normal activities; symptoms that require no medication or a medical evaluation; and transient signs and symptoms.
Unexpected AEs are those events, the specificity or severity of which is not consistent with the risk information described in the general investigative plan or the IRB proposal. "Unexpected" refers to an AE that has not been previously observed.
Expected AEs are those events, the specificity or severity of which is consistent with the risk information described in the general investigative plan or IRB proposal.
An UP includes any incident, experience or outcome that meets all the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the population being studied;
- Related or possibly related to participation in the research; and
- Suggests that the research places study participants or others at a greater risk of harm than was previously known or recognized.

An incident, experience, or outcome that meets all three criteria above will warrant DSMB/SMC consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions to protect the safety, welfare, or rights of participants or others.

Collection and Reporting of Adverse Events

Any event that meets the definition for an UP, AE, or SAE will be reported to the MPIs by research staff as soon as they learn about the event. Throughout the study, research staff will collect and document any UP, AE, or SAE using an Adverse Event Report that will include the following information:

- Identifying information for the research protocol, including the project title, names of MPIs, and the IRB project numbers;
- Participant study ID #;
- Date reported
- Brief description of the event;
- Date and method by which the MPIs were notified;
- Whether the event was related to participation in the study; and
- Action taken by the study team (instruction to inform PCP about the event)

SAEs will be reported to the IRBs within 48 hours by phone or email and a completed Adverse Event Report (Tables 1-3) will be submitted within 10 days of the initial IRB notification. Any SAE, whether related to study intervention or not, will be reported to the IRB and the DSMB/SMC. The MPIs will inform the IRB and DSMB/SMC immediately and jointly decide whether the reported event is a SAE that must be reported to the appropriate Federal Agency.

In the event that a participant either withdraws from the study or the investigator decides to discontinue them due to SAE, the participant will be monitored by the investigator via ongoing status assessment until 1) a resolution is reached, i.e., the problem requiring hospitalization has resolved or stabilized with no further changes expected; 2) the SAE is determined to be clearly unrelated to the study intervention; or 3) the SAE results in death. The outcomes of SAEs will be periodically reported to the IRB and to the funding agency. A summary of the SAEs that occurred during the previous year will be included in the annual progress report to the IRB and the DSMB/SMC. The report will include the participants' sociodemographic characteristics, expected versus actual recruitment rates, treatment retention rates, any quality assurance or regulatory issues that occurred during the past year, summary of AEs and SAEs, and any actions or changes with respect to the protocol.

Participant number	AE	Onset Date	Asthma-related	*Severity	*Relatedness to Study	*Action	Comments

*See Table 2

Table 2. Adverse Events Coding			
Asthma-related	Severity	Relatedness	Action Taken
0 = No 1 = Yes	1/2=mild/moderate 3/4=severe/ life threatening	0=Definitely unrelated 1=Unlikely 2=Possibly related 3=Probably related 4=Definitely related	0 = None 1 = Referral to Health Center for evaluation 2 = Referral to Emergency Evaluation

Table 3. AE Reporting Timeline

What Event is Reported	When is the Event Reported	By Whom is Event Reported	To Whom is Event Reported
Fatal or life-threatening unexpected SAE	Within 2 calendar days of initial receipt of information	PI	DSMB Institutional IRB NINR Program Officer
Non-fatal, non-life-threatening expected AE	Within 7 calendar days of initial receipt of information	PI	DSMB Institutional IRB NINR Program Officer
Unanticipated problem (UP) that is not a SAE	Within 15 calendar days of the investigator becoming aware of the problem	PI	DSMB Institutional IRB

We will register this trial with clinicaltrials.gov (*https://clinicaltrials.gov/*).

Frequency of Data and Safety Monitoring

The MPIs will be responsible for ensuring participants' safety on a daily basis. The protocol will be overseen by the DSMB/SMC. The MPIs and/or other study Co-Investigators will review all data collection forms throughout the study for data completeness and accuracy as well as protocol compliance. The DSMB/SMC will act in an advisory capacity to the MPIs to monitor participant safety, evaluate the progress of the study, and review procedures for maintaining the confidentiality of data and the quality of data collection, management, and analyses.

Reporting Mechanisms of IRB Actions to NIH

The IRB has authority, under HHS regulations at 45 CFR 46.109(a), to require, as a condition of continued approval by the IRBs, submission of more detailed information by the MPIs about any AE or UP occurring in a research protocol. If the IRB determines that the incident, experience, or outcome does not meet the above criteria for a UP, further reporting to the NINR Program Official would not be required under HHS regulations. Any IRB action taken because of this study will be reported to the NINR Program Official within 5 business days of notification. Any modifications to the Human Subject Research or Data Safety Monitoring Plan will be submitted for approval to the NIH Program Official prior to implementation of the change.

Reporting Mechanisms of Protocol or Consent Changes

Any proposed changes to a research study in response to an UP must be reviewed and approved by the IRB before being implemented, except when necessary to eliminate apparent immediate hazards to study participants. If the changes are more than minor, the changes must be reviewed and approved by the convened IRBs (45 CFR 46.103(b)(4) and 46.110(a)). Any IRB action taken because of this study will be reported to the NINR Program Official within 5 business days of notification.

Any protocol revisions or consent changes made in response to an UP must be approved by the IRB and the DSMB/SMC. As such, the MPIs will submit such changes to the IRB and DSMB/SMC for approval within 3 business days of identification of required changes. Any revisions involving a change in the scope of the study (e.g., risk to study participants) require prior authorization by NINR. Therefore, the MPIs will report such revisions to the Program Officer for approval. Protocol revisions and consent changes must be implemented within 5 days of IRB approval.

10.1.5 DATA HANDLING AND RECORD KEEPING

10.1.5.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

The research material obtained from each participant includes paper and electronic surveys, paper diaries, lung function tests (if in-person visits are allowed), spreadsheets, and audio files. Data obtained for the research project will not become part of the participant's health record. Only individuals who are members of the study team, or as mandated by the IRB or funding agency, will have access to coded or identifiable data. All materials will be collected specifically for the proposed research project. There is no planned collection of specimens.

Due to the likelihood of low health literacy, all forms will be administered to the patient participants or actively assisted. Trained Research Assistants (RAs) will enter responses into REDCap, a web-based electronic data capture system that is compliant with all regulatory requirements, after the visit. Audio files from intervention visits and post-trial interviews will be uploaded to a secure web platform and deleted from the recording device once transcripts are verified. Lung function results will be deleted from the spirometer's memory once a printout has been made and data has been entered and verified.

10.1.6 PUBLICATION AND DATA SHARING POLICY

Data Sharing Plan

The Principal Investigator will ensure that all datasets provided will be prepared in accordance with National Institute of Nursing Research (NINR) requirements for data repository of Common Data Elements and associated documentation as outlined in the NIH Data Sharing. We will submit data sets and variable and scale dictionaries to the NINR Program Official no later than 3 years after the end of the clinical activity (e.g., final participant follow-up) or 2 years after the main paper of the trial has been published, whichever comes first. The proposed research will include data from 110 minority caregivers and 110 of their children (aged 10-14) from New York City federally qualified health centers (FQHCs). The final dataset will include repeated measures of self-reported data from surveys completed by the participants that assess demographics, asthma-related outcomes and behaviors, and intervention adoption and maintenance. We will maintain data in storage for six years after publication of main findings to be able to respond to any requests from the scientific community. We are not producing any reagents or obtaining specimens such as DNA or other tissues. Nevertheless, we will assist other investigators to the best of our ability to conduct replication studies or studies that may extend our findings by making available whatever measures we are able to provide without violating legal restrictions such as copyright, trademark, or patent laws. We will facilitate access to data, provided investigators are approved to receive data by their home Institutional Review Board (IRB), the Western IRB or and the Columbia University IRB.

We agree with the NIH data sharing policy that data must be provided in a manner that protects the identity and privacy of study participants. To that end, only data de-identified by HIPAA standards will be released, and we will do our best to facilitate provision of such data, subject to availability of resources to support such sharing. To further protect participants, we will make the data and associated documentation available to users only under a data sharing agreement that provides for (1) a commitment to using the data only for research purposes, (2) a commitment to securing the data using appropriate encryption technology, and (3) a commitment to destroying or returning the data after analyses are completed. We will participate in any NIH data repositories that may become available, which would request and accept the data to be obtained through this project to hasten the tempo of scientific inquiry. We will work closely with the NINR to ensure full compliance with all requirements while preserving the privacy of individual participants.

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