PROTOCOL & STATISTICAL PLAN

Title: Air Quality Index (AQI) and Childhood Asthma: an intervention

NCT: 004454125

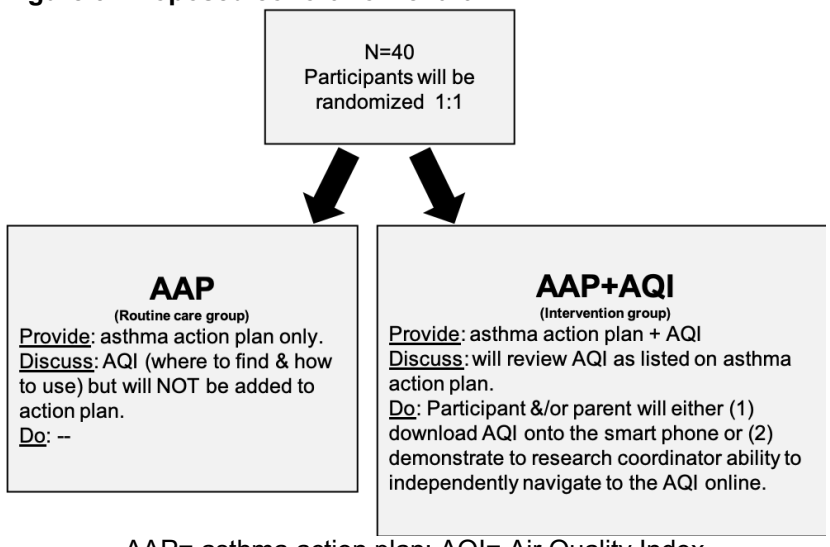
Date: March 17th, 2020

Note: The protocol and statistical plan were IRB approved on 03_17_2020. The following changes were made on 03_18_2022 prior to uploading to ClinicalTrials.gov: the protocol and statistical plan were combined and the protocol background and significance section were removed.

2. **STUDY DESIGN**:

Longitudinal (6 month) intervention trial, simple randomized 1:1 with stratification based on age (8-12 years, 13-17 years), non-blinded, to determine if adding the AQI to asthma action plans (AAP) reduces asthma exacerbations, and improves asthma control and quality of life (Figure 3).

Figure 3: Proposed cohort flow chart



AAP= asthma action plan; AQI= Air Quality Index

Both groups will receive basic education about the AQI including what the AQI is, where to find it, how to use it, and behavioral recommendations by category. In our practice, discussion of the AQI varies by practitioner and patients. While true routine care is likely absence of discussion of the AQI, this was determined to be inappropriate for this study. First, consenting children to the study would result in some discussion of the AQI and therefore bias any true "routine care". Second, we did not wish to withhold potentially vital asthma self-management to participants. Therefore, all children in the study will receive AQI education. The routine group will receive written AAP only, and the intervention group will receive AAP + AQI written plan. Additionally, the intervention group will be required to download the app onto their or their parent's smartphone (available both for iPhone or android phones) ***or*** demonstrate the ability to navigate to the airnow.gov website to obtain the AQI at their location. Participants will be followed at monthly intervals for 6 months.

The goal of the AQI is to familiarize persons to their own sensitivities to air pollution and encourage self-modification as needed for personal symptom control. Additionally, there is a goal to prevent discouraging physical activity as most US persons do not meet current daily recommendations.

2.1 Hypothesis and Specific Aims

We hypothesize that the addition of the AQI to AAP will (A) reduce asthma exacerbations, and (B) improve symptom control & quality of life in children with asthma. To test these hypotheses, in this study we will pursue the following specific aims:

- Aim 1: To recruit a pilot cohort of 40 children with asthma. For proof of concept, we will recruit 40 children with asthma from Children's Hospital of Pittsburgh, the only children's hospital serving southwest Pennsylvania (metropolitan area >2.6 million people). Baseline knowledge about the AQI including familiarity, usage, and prior healthcare provider discussion will be assessed.

- Aim 2: To evaluate if the addition of the AQI to AAP reduces asthma exacerbations in a pilot study of children. Participating children (Aim 1) will be randomized to one of two groups. All participants/caregivers will receive an AAP and verbal AQI education. The intervention group will additionally demonstrate the ability to check the AQI, and AQI recommendations will be incorporated onto their written AAP. Children will be followed monthly for 6 months to evaluate adherence to AQI recommendations and assess the frequency of asthma exacerbations, defined per ATS guidelines. Other known factors contributing to asthma exacerbations, such as asthma severity, viral illnesses, allergic triggers will also be monitored.

- Aim 3: To examine whether the addition of the AQI to AAP improves asthma symptom control and quality of life in a pilot study of children Asthma symptom control will be measured in participating children monthly, and quality of life will be assessed before randomization and at 6 months. Symptom control and quality of life will be evaluated within (before/after intervention) and between groups.

2.2 Outcome Measures

- **Asthma exacerbations** will be defined by ATS guidelines as:
  (1) Severe:
    a) requiring 3 or more days of systemic corticosteroids
    or
    b) ED visit/hospitalization for asthma treated with systemic steroids (any duration)

  (2) Moderate**:**
    a) asthma symptoms + increased rescue medication both for at least 2 days[50]
    or
    b) a visit to ED/urgent care/doctor office or clinic for which sick care was sought for asthma but no systemic steroids were given

  (note: Inclusion of urgent care/doctor office or clinic for acute asthma care is interpretation of PI and not explicitly stated in ATS guidelines, this does not include routine visits)

- **Asthma control** will be defined used validated asthma control tests: ACT for children 12 years and older and CACT for children 8-11 years.

- **Asthma quality of life** will be assessed via the validated pediatric asthma quality of life questionnaire (PAQLQ(S)).

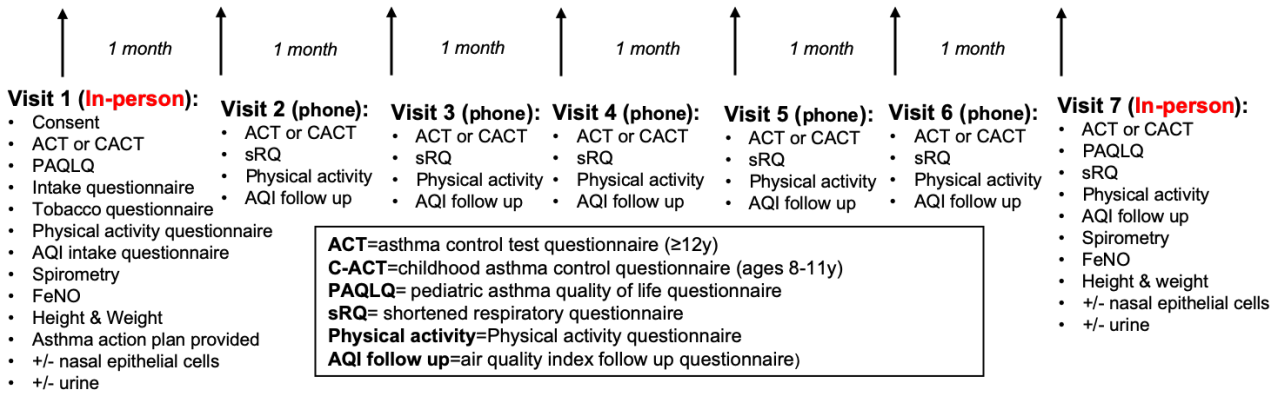
2.3 Questionnaires

7 questionnaires will be administered to the parents and children of study participants (see Figure 4). (**1**) Intake Questionnaire: this is a respiratory/general health questionnaire used by the [redacted] Study. **(2**) Tobacco Questionnaire- this is a short questionnaire from questions used on the National Youth Tobacco Survey. (**3**) AQI intake & follow up: Intake: there are no existing questionnaires evaluating what parents know about the AQI as pertains to their children with asthma. This questionnaire contains questions from NHANES and BRFSS with modifications. The AQI intake has a section to be completed by the parent to understand the parent's knowledge and practices regarding the AQI. The

intake questionnaire additionally contains a section for the child to complete, which is the AQI follow up questionnaire. The follow up questionnaire was developed by the PI to assess usage of the AQI. **(4)** Asthma Control Test (ACT)[51] and Childhood Asthma Control Test (C-ACT)[52] are validated questionnaires to assess asthma control in the last 4 weeks. (**5**) Pediatric Asthma Quality of Life Questionnaire (PAQLQ(S))© is validated questionnaire that will be interviewer-administered[53]. (**6)** Physical activity questionnaire contains modified questions from NHANES and The Physical Activity Questionnaire for older children and adolescents. **(7)** Shortened respiratory questionnaire (sRHQ): this is a short questionnaire that has been modified from the [redacted] study. It is designed to capture asthma exacerbations.

The order of the questionnaires is important. The AQI intake form will be completed by the parent/guardian and the child participant prior to AQI education/intervention.

Figure 4: Proposed cohort timeline by visit:



2.4 Lung Function Tests: Spirometry and fractional exhaled nitric oxide (FeNO) will be obtained at entrance and exit visit as secondary measures of control (e.g. forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV1), and FEV1/FVC).

2.5 Anthropometric measures: Height and weight will be obtained at the baseline and exit visit, to assess if adherence to AQI potentially alters weight/BMI by increased sedentarism.

2.6 Urine collection: as an ancillary to this study, will collect urine for cotinine measurement (nicotine metabolites) and store.

2.7 Nasal epithelial cells (NEC): as an ancillary to this study, NEC will be collected and stored for future studies aimed at understanding the effects of outdoor air pollution on epigenetic changes and how a behavioral intervention could alter impacts.

3. FUNDING:

The study is funded by the American Thoracic Society Foundation (ATSF) unrestricted pulmonary grant.

4. ORGANIZATION & LEADERSHIP:

The study's principal investigator is Franziska Rosser, MD MPH. Dr. Rosser is an assistant professor in the Department of Pediatrics, Division of Pulmonary Medicine. She is involved in clinical and research activities at UPMC Children's Hospital of Pittsburgh and recently served as a Co-Investigator on the [redacted].
Dr. Rosser is responsible for the study and will supervise training of study personnel, data collection, data collection quality, transition of study personnel, and human subjects protection. She will lead study meetings.

5. STUDY POPULATION:

The study will be recruited from and conducted at UPMC Children's Hospital of Pittsburgh (single site). Recruitment will be from pediatric pulmonology and pediatric asthma registry. Preference from asthma registry will be pediatric pulmonology clinic patients.

5.1 Inclusion Criteria:

Child participant:

1. Physician diagnosed persistent asthma (mild, moderate, or severe).
2. Aged 8-17 years old (at time of consent)
3. Family home internet access or smartphone access + willingness to download AirNow app on phone

Parent/guardian participant:

1. Parent or guardian of the child participant

5.2 Exclusion Criteria:

Child participant:

1. Diagnosis of other chronic respiratory disease (e.g. cystic fibrosis, bronchopulmonary dysplasia, etc.)
2. Immunodeficiency- acquired or congenital
3. Neuromuscular disease
4. Disability affecting ambulation (e.g. spastic quadriplegia)
5. Cyanotic congenital heart disease
6. Plans to move out of Pittsburgh area in next 6 months
7. Only 1 participant per household is eligible

Parental/guardian exclusion criteria: none

6. STUDY INTERVENTION:
All children will receive an asthma action plan (AAP). The asthma action plan lists the participant's daily asthma controller medications and informs patients/families what to do if asthma symptoms. All children will receive the same AQI education, however the intervention group will receive an AAP that has the reviewed AQI material printed on the back (Figure 5). In addition, the intervention group will demonstrate to research coordinator that (1) they can navigate to the airnow.gov website to check the local AQI ***or*** (2) they can navigate the AirNow phone app to check local AQI. (**see AQI education form**)

Figure 5: Back of AAP + AQI

Asthma checklist before going outside:

☑ ALWAYS keep your rescue inhaler (& spacer) handy

☑ Check the air quality index (AQI):
airnow.gov **OR** Airnow smartphone app

☑ Watch for symptoms: cough, wheezing, difficulty breathing, chest tightness.

☑ If you have symptoms, this is a sign to take it easy. Follow your yellow zone & consider: limiting time outside, increasing the number of breaks, do less intense activities, stop activity, or go indoors.

AQI	AQI #	What to do:
Good	0-50	No action required. A good day to be active outside!
Moderate	51-100	Children who are unusually sensitive to air pollution could have symptoms. If so, take steps to reduce prolonged or heavy exertion.
Unhealthy for sensitive groups	101-150	Ok to be active outside for short activities. For longer activities take mor breaks & do less intense activities. Reduce prolonged or heavy outdoor exertion.
Unhealthy	151-200	Move longer or more intense activities indoors. Avoid prolonged or heav exertion outdoors- a good day to work out in the gym.
Very Unhealthy	201-300	Move activities indoors. Avoid all physical activity outdoors.
Hazardous	301-500	Stay indoors and keep activity levels low. Keep windows closed and avoid frying/broiling on these days.

- Air pollution can make asthma symptoms worse and trigger attacks. Asthma symptoms can happe even on days when the air quality is good. Always keep your rescue inhaler handy.
- Exercising on days when air pollution is bad can mean more air pollution in your lungs. Changing your activity level can help. For example, take a walk instead of a run. Changing how long you spend outside exercising can also help. For example, don't stay outside as long.

Plan activities when and where pollution is lower:

- Ozone is usually higher on hot summer days in the afternoon & early evening. On days ozone is high, plan your outdoor activities in the morning.
- Particulate pollution can be higher in certain places. Try to avoid exercising where particles are higher. Examples: near busy roadways, during rush-hour traffic, near industrial areas, and when there is smoke in the air.

Don't let asthma keep you from being active. The CDC recommends 60 minutes of physical activity a day. If asthma is limiting your activity, talk to your doctor!

As mentioned above in Section 2, all patients will receive education about the AQI as we do not wish to withhold potentially valuable information and the consenting process will result in discussion of the AQI. However, the intervention group will be provided the AQI on the back of their AAP whereas the control group will not.

7. POTENTIAL BENEFITS:

This protocol will help to determine if improved education and usage of an already publicly available intervention (AQI) reduces asthma exacerbations, improves asthma control and asthma quality of life. If this intervention is effective there will be benefits for pediatric patients with asthma.

Parents and participants will be provided with an asthma action. All participants should already have an asthma action plan as part of their care, however there may be an additional benefit of providing the plan. The results of spirometry or FeNO may be shared with the participant's primary care physician or asthma specialist (per parental request/approval).

8. RISKS AND DISCOMFORTS:

8.1. Procedures

Table 1: Study Procedures					
VISIT	**LOCATION**	**QUESTIONNAIRE**	**EMR**	**MEASURES**	**SPECIMENS**
1	In-person, PCTRC	Intake, AQI intake, PA, ACT or CACT, PAQLQ, tobacco intake	Confirm asthma controller medications, IgE, allergen testing, eosinophila, BAL or sputum eosionphils	Spirometry, FeNO, height, weight	Nasal epithelial cells, urine
2	Telephone	sRQ, AQI_f/u, PA, ACT or CACT.	-	-	-
3	Telephone	sRQ, AQI_f/u, PA, ACT or CACT.,	-	-	-
4	Telephone	sRQ, AQI_f/u, PA, ACT or CACT.	-	-	-
5	Telephone	sRQ, AQI_f/u, PA, ACT or CACT.	-	-	-
6	Telephone	sRQ, AQI_f/u, PA, ACT or CACT.	-	-	-
7	In-person, PCTRC	sRQ, AQI_f/u, PA, ACT or CACT.	-	Spirometry, FeNO, height, weight	Nasal epithelial cells, urine
Intake questionnaire (completed by parent); AQI intake- includes parent portion (completed by parent) + AQI follow up (completed by participant); PA=physical activity (parent and/or participant), ACT=asthma control test ages 12 and older (completed by participant); CACT=childhood asthma control test for ages 8-11 (completed by parent and participant); PAQLQ(s)-pediatric asthma quality of life questionnaire (completed by participant); participant tobacco intake form (completed by participant); sRQ= shortened respiratory questionnaire (completed by parent); AQI_f/u=AQI follow up questionnaire (completed by participant).					

8.1a Questionnaires: the risks from questionnaire administration involves social-psychological risk resulting from inadvertent disclosure of medical information and/or questions may create discomfort. Participants and parents do not have to answer any question that they do not wish to answer.

8.1b Spirometry: The risks of spirometry are minimal and include temporary lightheadedness from repeated spirometry maneuvers and there is a small risk (rare) of wheezing and shortness of breath and increased cough when performing spirometry. If the participant has had a pneumothorax (a.k.a collapsed lung, air leak), open thoracic surgery (a.k.a open chest surgery), myocardial infarction (a.k.a heart attack), or hemoptysis (a.k.a coughing up blood) in the last 2 months they should not undergo spirometry.

8.1c Fractional Exhaled Nitric Oxide (FeNO): The risks of FeNO are similar to spirometry in that they are minimal may include temporary lightheadedness. If the participant has had a pneumothorax (a.k.a collapsed lung, air leak), open thoracic surgery (a.k.a open chest surgery), myocardial infarction (a.k.a heart attack), or hemoptysis (a.k.a coughing up blood) in the last 2 months they should not undergo FeNO.

8.1d Nasal epithelial collection: The main risk of the nasal sample is discomfort and nose bleeding. Additional risks include watery eyes and sneezing. There is also the rare possibility of a tear at the brushing site and infection from this procedure. We will place a small amount of lidocaine (~1cc) into the participants nose to reduce discomfort. Lidocaine will not be injected with a needle (no needles will be used). Lidocaine sometimes cause an unpleasant taste in the mouth and may cause temporary redness, stinging, and swelling at the application

site. If the participant has a bleeding disorder (coagulopathy) they should not undergo nasal cell collection.

8.1e Urine collection: the risks of urine collection are minimal and may include discomfort with providing a sample.

8.1f Measures of height and weight: possible participant discomfort with having weight obtained. The risks are minimal.

8.2 Break of confidentiality: participant data will be identified by a unique study number assigned to each child. The unique study number will be used as identification and not participant identifying information (ex. first name, last name, DOB) will be kept with research information. The link between study ID and participant will be kept in a secure and locked location.

8.3 Genetic testing: Genetic testing carries the potential for breach of confidentiality that could have a potential impact on future reproduction plans, insurability, employability, or could have a negative impact on family relationships, and/or result in paternity suits or stigmatization. Information about the child's participation and results will not be placed in the medical record. Participants will not be informed about an individual genetic data to be obtained from the study. Genetic information will never be labeled with a participant's identifying information such as name, date of birth, etc.

8.4 Study intervention:
There are no known risks associated with the AQI.

9. INFORMED CONSENT:

There is one consent form for both the parent participant and the child participant. Informed consent and child assent will be obtained after thorough discussion of the potential risks and benefits.

10. ADVERSE EVENTS:

10.1 Adverse events
The risk for adverse events related to the study intervention are minimal. An adverse event will be defined as an unexpected accident, experience, or outcome that is unexpected (in terms of nature, severity, or frequency), is related or possibly related to the subject's participation in the research, and places subjects or others at a greater harm (including physical, psychological, economic, or social harm) than was previously known or recognized. Such events will be recorded as per 45 CFR part 46. Unexpected adverse events of moderate severity will be reported to the IRB within 10 working days of the investigator learning of the event.

As asthma is a chronic lung disease with waxing and waning impairment and risk, asthma exacerbations (both severe & moderate) and loss of control are not unexpected. We will consider an increased severity or frequency of such events as adverse events, although these will not meet the definition required for reporting to IRB as these such events are not anticipated to be related or possibly related to the research.

Specific examples of these are below. While these will not require reporting to the IRB, they will be captured as adverse events and safety procedures will be implemented as below:

1. If a participant has more than 3 severe asthma exacerbations during the study
2. If a participant has 3 consecutive ACT or C-ACT scores ≤19.
3. If a participant has an FEV1 < 80% at either V1 or V7

These events will be recorded, parent or guardian/participant will be notified of possible poorly controlled asthma and will be encouraged to follow up with managing asthma specialist. With parental permission, PI or RC will reach out to managing asthma specialist to alert to concerns.

10.2 Serious Adverse Event

A serious adverse event will be defined as an event that is fatal, life-threatening, inpatient hospitalization or prolongation of hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.

As we anticipate learning of such events (e.g. hospitalization for asthma exacerbation) retrospectively (thru questionnaire) we will inquire about whether the participant has been seen by managing asthma specialist since event. If the answer is no, we will encourage family/participant to contact asthma specialist and with permission, PI or RC will alert managing asthma specialist.

Serious adverse events will be reported to the IRB within 24 hours of learning of any unexpected serious adverse event associated with the research intervention.

11. CLINICAL MANAGEMENT AND DATA COLLECTION:

Table 2: Summary of Study Protocol

VISIT	LOCATION	TIMING	QUESTIONNAIRE	MEASURES	SPECIMENS
V1	In-person, PCTRC	Start	AQI intake*, Intake, PA, ACT or CACT, PAQLQ, tobacco intake	Spirometry, FeNO, ht, wt	NEC, urine
V2	Telephone	W4, 4 wks post V3 (+/- 7d)	sRQ, AQI_f/u, PA, ACT or CACT.	-	-
V3	Telephone	W8, 4 wks post V3 (+/- 7d)	sRQ, AQI_f/u, PA, ACT or CACT.,	-	-
V4	Telephone	W12, 4 wks post V3 (+/- 7d)	sRQ, AQI_f/u, PA, ACT or CACT.	-	-
V5	Telephone	W16, 4 wks post V3 (+/- 7d)	sRQ, AQI_f/u, PA, ACT or CACT.	-	-
V6	Telephone	W20, 4 wks post V3 (+/- 7d)	sRQ, AQI_f/u, PA, ACT or CACT.	-	-
7V	In-person, PCTRC	W24, 4 wks post V3 (+/- 7d)	sRQ, AQI_f/u, PA, ACT or CACT.	Spirometry, FeNO, ht, wt	NEC, urine

Intake questionnaire (completed by parent); AQI intake- includes parent portion (completed by parent) + AQI follow up (completed by participant); PA=physical activity (parent and/or participant), ACT=asthma control test ages 12 and older (completed by participant); CACT=childhood asthma control test for ages 8-11 (completed by parent and participant); PAQLQ(s)-pediatric asthma quality of life questionnaire (completed by participant); participant tobacco intake form (completed by participant); sRQ= shortened respiratory questionnaire (completed by parent); AQI_f/u=AQI follow up questionnaire (completed by participant).
Ht=height, wt=weight, NEC=nasal epithelial cells
*AQI intake form should be completed prior to AQI education/intervention.

11.1 Recruitment

Recruitment will occur at UPMC Children's Hospital of Pittsburgh Pediatric Pulmonology and from Pediatric Asthma Registry. A referral log will be used to track the age and gender of every child whose family is approached about the study but declines or who is not eligible because of lack of home internet or smart phone access. The research coordinator will determine eligibility criteria (as much is possible) prior to reaching out to family about study.

11.2 Eligibility and Randomization (Visit 1)

Once the family and participant have indicated willingness to participate and have scheduled a V1, the research coordinator will notify PI. PI will review medical record (granted permission by Asthma Registry patients and allowable access as part of regular duties) to confirm asthma controller medications. PI will prepare AAP for research coordinators to distribute. In the event of a discrepancy between parental reported controller medication and medical record medication, the PI will reach out (with participant parent permission) to healthcare provider managing asthma to confirm asthma controller medications.

After informed consent has been obtained, participant's will be randomized 1:1 by age group. The RC assign random group at time of intervention. Eligibility for lung function tests and/or NEC will be assessed prior to study procedures. Questionnaires will be administered, height and weight will be obtained, lung function tests will be obtained (if eligible), specimens will be collected (if applicable), and AQI education will be provided. For the intervention group only, the AAP containing the AQI information will be provided. The intervention group will demonstrate ability to navigate to either airnow website or airnow app on smart phone. For the control group, an AAP will be provided (containing no AQI information) Both the participants, parents, and research coordinator will know randomization assignment. V1 should not be done if child participant has been sick with respiratory infection in prior 7 days or currently has respiratory symptoms.

If a participant's spirometry demonstrates an FEV1 <80%, the family and participant's managing asthma healthcare provider will be notified. Per family permission, spirometry will be shared with managing asthma healthcare provider. If a participant's FeNO is above 20ppb, with family permission, FeNO will be shared with managing asthma healthcare provider.

11.3 Trial Phase (Visits 2-6)

The participants will be followed monthly (every 4 weeks, +/- 7 days) with interval follow up telephone calls. Questionnaires will be administered during the telephone calls. Throughout the trial, participants will be reminded that participation in the research study does not replace clinical care. Moderate and severe asthma exacerbations will be asked about on monthly questionnaires. If a participant reports 3 severe asthma exacerbations (so defined by ATS criteria as an event requiring 3 or more days of systemic steroid treatment for asthma or an ED visit/hospitalization during which a steroid was prescribed), the participant's managing asthma healthcare provider will be notified. Additionally, if a participant has more 3 consecutive ACT or CACT scores that are equal to or less than 19, which is the threshold concerning for asthma control, the participant's managing healthcare provider will be notified.

11.4 Exit visit (Visit 7)

Visit 7 will be conducted in person. Eligibility for lung function tests and/or NEC will be assessed prior to study procedures. Questionnaires will be administered, height and weight will be obtained, lung function tests will be obtained (if eligible), and specimens will be collected (if applicable).

If a participant's spirometry demonstrates an FEV1 <80%, the family and participant's managing asthma healthcare provider will be notified. Per family permission, spirometry will be shared with managing asthma healthcare provider. If a participant's FeNO is above 20ppb, with family permission, FeNO will be shared with managing asthma healthcare provider.

11.5 Protocol Violations

Protocol violations are defined as departures from accepted clinical research practices, study protocol, and/or study procedures that pose a risk to participant safety, adversely affect data quality and the integrity of the major scientific goals of the study, and/or involve a significant and repeated breach of participants' privacy. Protocol violations include (but are not limited to):

- Failure to obtain informed consent appropriately
- Enrollment and/or randomization of ineligible participants
- Incorrect intervention provided to participant
- Failure to follow the protocol safety monitoring plan
- Breaches of confidentiality resulting from lost, misplaced, or stolen study documents.

By the nature of their definition protocol violations are considered the most serious class of departure from the study protocol.

11.6 Protocol Deviations

Protocol deviations are defined as departures from a study protocol or methods of a procedure that do not pose a risk to subject safety, do not adversely affect the integrity of the major scientific goals of the study, and do not involve a significant and repeated breach of participant privacy. Protocol deviations include (but are not limited to):

- Mistimed procedures
- Omission of protocol and/or procedure elements that do not impact participant safety
- Failure to carry out study procedures in the appropriate order, when applicable
- Submission or an outdated version of a data collection form

All protocol violations and deviations will be reported at the time of discovery to the PI. PD reports will be reviewed at regular meetings, no less than monthly.

12. SPECIMEN HANDLING

If applicable, NEC and urine will be obtained at Visit 1 and 7. NEC will be processed and stored in the laboratory of [redacted] located in Rangos Research Building. Urine will be stored and processed in the laboratory of [redacted].

13. DATA MANAGEMENT

13.1 Electronic Data Entry

Research coordinators will endeavor to enter all information into redcap at time of visits. If paper forms are used, they will not contain personal identifiers and should be entered immediately into redcap as soon as possible.

13.2 Data Quality

All data should be entered into Redcap. Questions will be labeled as required as to trigger an alert to the research coordinator upon saving if there are missing questions. Participants may choose not to answer any question.

13.3 Privacy and Data Security

Procedures will be implemented to maintain the security and confidentiality of participant data, including assigning unique study identifiers rather than using names or other identifying information.

Participant records will kept in accordance with IRB-approved consent procedures, and thereafter destroyed leaving available only de-identified data for use in publications, presentations, etc.

14. DATA SAFETY AND MONITORING:

Dr. Rosser will oversee this clinical study thru close contact with research coordinators and close monitoring of data. Dr. Rosser will review recruitment, enrollment and study visit data.. Study procedures will be reviewed and monitored by PI. All deviations/violations will be reported as per IRB specifications.

The risks of this study are minimal.

Please refer to adverse event section regarding reporting to the IRB. As noted in prior section, children with asthma are expected to have asthma exacerbations and loss of control. Should such events be deemed to be outside frequency or severity, contact will be made with participant’s parent/guardian and with permission, PI or RC will reach out to asthma managing specialist to alert to potential concerns. Participants/families will be reminded at each visit that participation in this study does not replace clinical asthma care. All concerns about asthma control or management will be encouraged to be discussed with the participant’s asthma care provider.

STATISTICAL PLAN:

Statistical Analysis: Data will be analyzed using SAS (SAS 9.4, Cary, N.C.). Baseline statistics per treatment group will be obtained. Bivariate analysis of covariates (age, sex, race/ethnicity, asthma severity, phenotype (i.e. atopic), socioeconomic status (SES), exposure to primary or secondary tobacco smoke, FeNO, use of controller medication, etc) between groups will be conducted using student t-test or Wilcoxon rank sum and Fisher's exact or Chi-square (where appropriate and based on distribution). Variables with significant differences between groups ($P<0.05$) will be considered for inclusion in multivariate model selection. The effects of physical activity on the outcomes will be compared between groups. Baseline knowledge and usage of AQI will be assessed. Adherence to AQI will also be assessed and compared between groups, with potential stratification by AQI usage. Additionally, differences in weight and BMI will be assessed to evaluate if adherence to AQI promotes sedentarism and leads to increased weight gain. We will evaluate our outcomes (Aims 2 and 3) in three ways. First, we will evaluate the average difference (overall mean) between groups for our primary outcomes using T test or chi-square (where appropriate). Additionally, we will test the average mean difference between each treatment group by multivariate regression (linear for PAQLQ and ACT or CACT, and/or Poisson or logistic regression for mean asthma exacerbations depending on distribution) to allow for covariate adjustment. Second, we will use paired t-tests (or matched Wilcoxon signed-rank) to evaluate the within group effects (6 month mean – baseline) for each primary outcome. Third, to assess the effects over time in our intervention study (correlated repeat measures data), we anticipate analyzing our primary outcomes by generalized linear mixed models (GLMM). For these models, we will first evaluate the distribution of our primary outcome and determine the most appropriate link (e.g. for severe asthma exacerbations: logistic link if there are overall a high proportion of participants with none, or Poisson link if more consistent with count data). A stepwise approach will be used to build all multivariable models. All final models will include age, sex, race/ethnicity, SES, and tobacco smoke exposure. Additionally, the above outcomes will be stratified by age group (8-12y, 13-17y) to determine if the effects are greater in older children for whom the AQI recommendations may be better self-incorporated into outdoor physical activities, vs the younger group who will likely be more reliant on parental checking and activity modification.

Power calculations: Power calculations were conducted using G*Power 354 and SAS (SAS 9.4, Cary, N.C.) using proc glmpower. For mean difference between treatment groups (routine vs. intervention) with sample size of 20 participants per group, two-tailed test, alpha 0.05, we will have ≥90% power to detect a mean difference of 1.05 between groups for mean asthma exacerbations, ACT and C-CACT, and PAQLQ. Our study will provide ≥80% power to detect a mean difference of 0.91. As the clinical difference for ACT is 2-3 points, we anticipate adequate power to detect a clinical difference. The estimated clinically meaningful difference in PAQLQ is 0.5, and our study may be underpowered to detect this small of difference with this analysis. For comparison within each treatment group, comparing the matched difference (end of study- baseline), using the same assumptions above, we will have ≥90% power to detect a mean difference of 0.76, and ≥80% power to detect a mean difference of 0.66. Therefore, we expect better ability to detect changes in PAQLQ within the groups then between them. For repeat measures, we estimated our power using proc glmpower using F test based on Hotelling-Lawley trace. We estimated a study allocation of 1:1, alpha 0.05, repeated measures at 1, 2, 3, 4, 5 months, lear correlation structure with base correlation 0.85 & decay rate of 1, with an estimated mean difference of 2, standard deviation of 2, which provides a ≥90% power for a treatment group size of 12 for overall mean and n=26 for time*treatment.