Symptom Perception, Behavior, and Outcomes in Older Asthmatics
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Mount Sinai	Protocol Name:	Symptom perception, behavior, and outcomes in older asthmatics
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	Date Revised:	1/7/2021
	Study Number:	15-0667

HRP-503 Application (Protocol Supplement)

- *This application can only be used in conjunction with a protocol. If this project does not have a protocol from the sponsor or is already included in a grant application then a comprehensive protocol should be developed. A comprehensive template and online wizard is located at: NIH Wizard.*
- *Note that, depending on the nature of your research, certain questions, directions, or entire sections below may not be applicable, or may have been fully covered in the protocol. Provide information if and when applicable. If the answer is found in the protocol please provide a page reference. If the question is not applicable to the study, mark the section "N/A". Do not delete any sections.*
- *Be sure to complete any supplement questions from one or another ancillary office that you receive during the RUTH application process. Please make certain that the protocol, this 503 application and responses to ancillary offices do not contradict each other and the information is incorporated in all documents where appropriate. Be sure to save the Ancillary office responses you provided within RedCap and upload them to Ruth.*
- *Throughout this application are references to checklists. These tools are used by the IRB to make specific regulatory findings. To allow us to do that it is the applicant's responsibility to ensure that your protocol has sufficiently addressed these additional regulatory criteria for approval, and that the applicant identifies those protocol specific findings required by the checklist. how will they do that, here or a separate form?*
- *Keep an electronic copy of this version of the document. You will need to modify this copy when making changes.*

1. Setting of the Human Research:

- Mount Sinai Locations: Icahn School of Medicine at Mount Sinai, Mount Sinai Beth Israel, Mount Sinai St. Luke's, Mount Sinai West, Internal Medicine Associates, other
- External Study Locations: Jacobi Medical Center, Montefiore Medical Center

2. Resources Available to Conduct the Human Research: (the aim here is to assess if the research is likely to be successful and thus justify the efforts and risks taken by the subjects):

- We demonstrated the feasibility and validity of the proposed symptom perception methodology and clinical accuracy grid by showing that asthma symptom perception was associated with asthma morbidity across a 1-year follow-up.15 Estimates of PEF as a measure of asthma symptom perception is more accurate than verbal descriptors (e.g.,

difficulty with breathing) to communicate dyspnea when compared to actual PEF values.123 The PEF self-estimate provides a common language that minimizes cultural differences in descriptors of dyspnea, which have been shown to vary by ethnicity.124,125 We found that there are no ethnic differences among Puerto Rican, African-American, and Afro-Caribbean children with asthma on symptom perception accuracy using the proposed methodology or in response to our PEF prediction with feedback intervention.14We will recruit participants from general medicine and pulmonary outpatient clinics in the Mount Sinai Health System, at Jacobi Medical Center, and Montefiore Medical Center.

3. Study Design:

a) Recruitment Methods (see PPHS policy):

- Potentially eligible participants will be identified through monthly queries of the patient registration systems. The RAs will obtain permission from physicians to contact these patients. Emergency Department (ED) Recruitment: ED recruitment will increase enrollment of individuals who may use the ED as their usual source of care. RAs will query the ED's electronic registration system and will monitor the asthma treatment areas to identify potentially eligible patients. Once a potential participant is identified, the RAs will obtain permission from the ED physician and follow the steps described above. Please note that subjects will not require consent from a Primary Care Provider separate from their ED provider in order to participate in the study.
- We will recruit and introduce the study to participants using the following steps:
    - Obtain approval from physician. Physicians will be asked if we may approach all the eligible patients under their care, if we may approach a patient under their care on a patient-by-patient basis, or not approach their patients. We will contact the primary care provider or pulmonologist primarily responsible for patients' pulmonary care. A physician's decision will be documented by either a signed Physician Approval Form or via email.
    - Research team approaches patient. There will be no "cold contact" of potential participants. Participants will first receive a letter which will introduce them to the study and give them the opportunity to opt out. If they do not choose to opt out, ten (10) days after the letter was mailed, an RA will approach the patient over the telephone. RAs will use an IRB approved recruitment script. If the patient is interested in the study, the RA will confirm that they meet eligibility criteria. Patients who screen eligible will be offered participation and schedule the baseline interview. On the day of the baseline, the RA will meet with the subjects and administer the

informed consent procedure before any data is collected for research purposes.

- Alternatively, interested patients may contact the research team through the phone number provided in the letter.
- Participants interested in the study who would like more information before deciding to enroll will be provided with an informational brochure, which includes an overview of the study as well as the research team's contact information.

b) Inclusion and Exclusion Criteria:

- At Mount Sinai the eligibility screening process will begin with reviewing the medical records of potentially eligible patients identified by the Data Warehouse. Patients who are eligible based on their medical record will be contacted first by letter and then by phone. If the patient is reached over the phone, the RA will verify the patient's age, asthma history, and that the patient does not meet exclusion criteria. A HIPAA waiver has been obtained for this study.
- At the Albert Einstein College of Medicine, patients are first contacted by letter and then by phone. If the patient is reached over the phone, the RA will verify the patient's age, asthma history, and that the patient does not meet exclusion criteria. At that point, then medical records are reviewed to confirm that the person is eligible.
- Inclusion Criteria:
  a. Age greater than or equal to 60 years
  b. English or Spanish speaking
  c. asthma diagnosis made by a health care provider
- Exclusion Criteria:
  a. Diagnosed with chronic obstructive lung disease (COPD) or other chronic respiratory illness;
  b. Smoking history greater than or equal to 15 pack-years (to exclude undiagnosed COPD);
  c. dementia;
  d. moderate or severe cardiac disease (including New York Heart Association stages 4 or 5 congestive heart failure, because dyspnea among patients with severe heart failure is more likely to be attributable to their heart condition than their asthma);
  e. dependence on assistance for medication administration since we are focused on SMB;.
  f. uncorrectable visual impairment since the cognition assessments require vision

c) Number of Subjects:

- Number of subjects to be enrolled is 400 across 3 study sites
  a. Mount Sinai – 200

b. Montefiore Medical Center – 100
c. Jacobi Medical Center - 100

d) Study Timelines:

April 1, 2016-March 31, 2021; participants will be enrolled for a 15-month period

Table 1. Study Timeline

TASK	YR 1		YR 2		YR 3		YR 4		YR 5	
Train RAs, pilot, translations										
Baseline interviews										
Follow-up interviews/Pilot										
Data Analysis										
Dissemination/manuscrip										

e) Specimen Banking for Future Uses Not Part of This Project:

N/A

f) Data Storage, Transmission and Confidentiality:

Icahn School of Medicine at Mount Sinai (ISMSS) will serve as the data-coordinating center. The study teams at ISMMS, Jacobi Medical Center and Montefiore Medical Center will work together on recruitment. The teams at all sites other than ISMMS will recruit participants from their sites only and will only have access to data from their site. Once the data is collected, those teams will send the de-identified data to the Mount Sinai team, who will then combine that data with the data from Mount Sinai participants

g) Data and Safety Monitoring Plan:

- **For projects with a Data Safety Monitoring Board/Data Safety Committee (DMSB/DMC)**:

Brief description of the DSMB: The DSMB will be formed before the pilot study begins. We will convene a DSMB to oversee patient safety for the pilot intervention proposed for Aim 3. The board will consist of a primary care physician, a pulmonologist, a biostatistician, and a behavioral health research scientist. The board members will meet prior to implementation of the pilot RCT of the intervention to review the study protocol and measures to ensure that adequate protections and the plan to monitor for adverse

events are adequate. They will then meet every 6 months after implementation of the pilot to review data, including the following elements: recruitment rate, study withdrawal, reasons for withdrawal, adverse events, impact of intervention on beliefs and behaviors.

Qualifications of DSMB members: The DSMB will consist of a primary care physician, a pulmonologist, a biostatistician, and a behavioral health research scientist. The board will not serve as co-investigators on the study. A DSMB chair will be identified and will convene the board every six months to review the study and accumulated data.

Role and Responsibilities of the DSMB: The DSMB is an independent group advisory to the MPIs and is required to provide recommendations about starting, continuing, and stopping the study. In addition, the DSMB is asked to make recommendations, as appropriate, to the MPIs about:

- Efficacy of the study intervention
- Benefit/risk ratio of procedures and participant burden
- Selection, recruitment, and retention of participants
- Adherence to protocol requirements
- Completeness, quality, and analysis of measurements
- Amendments to the study protocol and consent forms
- Participant safety
- Notification of and referral for abnormal findings

The DSMB will monitor patient safety, consider new scientific or therapeutic developments that could impact safety or trial ethics, and make recommendations to continue, terminate, or modify the trial based on interim analyses. The DSMB will specifically review: 1) hospitalization and mortality rates; 2) study disenrollment unrelated to death; 3) any patient, caregiver, and healthcare provider concerns. The DSMB may recommend stopping the trial if there is clear evidence of harm or overwhelming benefit. Adverse events will include disruption of previously established regular care such that the patient's health is jeopardized or excessive burden created by the time required to participate in the study. The DSMB can recommend changes in study protocol or termination of the study if it concludes the study design causes disruptions in patient-provider continuity which jeopardized the health of the study subject or if the study imposes excessive burden on patients. Finally the DSMB, at the request of the sponsor, will review accrual and evaluate study progress towards meeting recruitment targets.

The DSMB will review safety and data information every 6 months. Should a temporary or permanent suspension of the study occur, in addition to the PPHS, we will report this to NIH.

h) For other projects with greater than minimal risk a monitoring plan must be provided:

N/A

i) Withdrawal of Subjects:

- Participants have the right to withdraw from the study at any time. Participants may withdraw through written or phone request to the Principal Investigator or research staff.
- The principal investigator, the sponsor or the institution may stop the participant's involvement in this research study at any time without consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in the participant's best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without the participant's consent.

4. Provisions for Research Related Harm/Injury:

Participants will be at minimal risk and have the right to withdraw from the study at any time. Members of the research team are bilingual, so outside interpreters will not be needed for recruitment, data collection, or coding. As in prior studies, we will include questions at the end of this survey to identify participants at risk of harm or worsening health. Those participants identified will be referred to a designated social worker (individuals with acute needs) or services available in the community. Since issues of patient safety are inherent in assessments for depression, we created protocols that will be in place for research staff to follow, should a patient endorse and/or be found experiencing suicidal ideation, whether with plan and intent or not. If patients with suicidal ideation are identified, this protocol requires that the PIs and/or a senior psychology/psychiatry staff member are notified and based on the patient's presentation and history a determination is made as to whether the patient is safe to participate in the study and/or whether a formal consult for psychiatric care is necessary. We will also adhere to these protocols at each follow-up contact. Participants who screen positive for depression but do not have suicidal ideation will be given a list of counseling sites serving their community and offered referral for psychological counseling at the research sites.

During spirometry testing, participants will be instructed to alert staff if they feel lightheaded or dizzy. Those who report symptoms will be promptly instructed to discontinue the test and sit down. A physician will be available at all times to assess the patient if symptoms persist.

5. Recordings:

- Will any video or audio recordings be made for research purposes? Yes
- All audio and video recordings will be accessible only to the research team and will be stored on or secure drive. Any recordings transmitted between sites will be sent securely via OneDrive.
- Data will be stored for 7 years following the completion of data analysis.
- Research staff will inform the participant before beginning the interview if they intend to record and will ask the participant for permission before recording. If the participant does not wish to be recorded, they may still participate in the interview and the session will not be recorded.

6. Provisions to Protect the Privacy Interests of Subjects:

To protect the privacy interests of subjects, all communications with study subjects will be via face-to-face visit, HIPAA compliant zoom, telephone or email. Phone messages left will not refer the study in which they are enrolled but only the site where they were enrolled. For example, we would leave a message such as, "This is XXXX calling from Mount Sinai." Patients will be asked whether they prefer phone contact or email contact for their follow-up.

Protection of subject privacy. To preserve patient confidentiality, study subjects will be assigned code numbers. Using these codes, none of the collection forms will contain the names or medical record number of the patients or other personal identifiers. There will be a master list at each institution matching the names of the patients to the code numbers. The list will be safely stored in secure network drives. Paper-based consent and HIPAA documents will be stored in locked cabinets within locked offices, separate from the master lists. All electronic data will be stored on mainframe servers, and terminals and Tablet PCs will be password protected and maintained in locked offices.

Database protection. Patient information will only be accessible to the MPIs, project manager, and research coordinators associated with the research. Data collected on Tablet personal computers (PC) will be uploaded on a daily basis to mainframe servers supported by the local institutions and encrypted using Bitlocker software. These data will lack personal identifiers other than a study identification code. Following the upload, the data on the Tablet PCs will be deleted. Encrypted data from the JMC and MMC sites will be transferred electronically to Mount Sinai, which will serve as the data coordinating center, on a weekly basis. The transferred data will be free of personal data that

qualifies as PHI. All data received at the data coordinating center (Mount Sinai) will be entered into a computerized database and stored in encrypted files on a mainframe server that is backed up nightly by the Mount Sinai Hospital IT Department.

Confidentiality during adverse event reporting. Adverse event reports and annual summaries will not include subject-identifiable material. Each will include the coded identification number only.

7. Economic Impact on Subjects:

No cost, besides transportation costs associated with in-person study visits, are expected.

8. Payments/Reimbursements to Subjects:

Study participants may receive up to $310 for participating in the study. Study participants will receive $50 via cash or money order after the completion of the baseline interview. An additional $20 will be given to the participants after they return the electronic monitoring device for the medication and the electronic peak flow meter. Participants will receive $40 in cash/money orderafter the completion of each follow-up interview (6 months and 12 months). An additional $20 will be given to the participants after they return the electronic monitoring device for the medication and the electronic peak flow meter after each follow up interview. In addition, if participants participate in the pilot study, they we will receive $20 in cash/money order after the completion of the first interview (12.5 month visit) and $30 for each of the follow-up interviews (14 months and 15 months). An additional $20 will be given to the participants after they return the electronic monitoring device for the medication and the electronic peak flow meter after each pilot interview. Payment for each interview and device return is not contingent upon the completion of the entire study. Study participants will be paid in cash/money order for returning their devices at the next visit unless otherwise requested. If patients receive a device at the 15-month pilot visit and return it (or any other visit if they choose to withdraw before completing the study), they will be paid by money order for returning that device.

9. Consent Process:

- Written or verbal informed consent will be obtained from each subject at entry into the study. Written informed consent is obtained by the following process:
  - *Subject reviews the study consent form.*
  - *MPIs or research delegates speak with the subject to review the consent, confirm subject's understanding, and answer any questions.*

- *Once the investigator is convinced that the subject verbally demonstrates understanding and agrees to the process, the consent is signed by the subject and/or the research delegate. Individuals authorized to obtain written consent are the principal investigators, co-investigators, and assigned research delegates specifically designated by the principal investigators to work on this project.*

- For any subject being consented via phone or a HIPAA complaint Zoom platform we will follow the below procedure:
  - *Send the IRB approved informed consent formto the prospective research subject for review.*
  - *Arrange for a conversation between the participant and an authorized member of the research team to allow for full discussion of the informed consent form. If verbal consent is obtained, collect identifiable data as applicable.*
  - *If there is an adult witness on the phone at the time of the initial verbal consent, the documents will not be returned.*
  - *If there is no adult witness to the phone consent, the written document will be requested to be returned via regular mail, fax, or email. If after two weeks, the signed document is not returned the data will be stripped of all identifiers and links such that the de-identified data are permanently anonymized.*

There is no waiting period for obtaining consent.

The SOP HRP-090 Informed Consent Process for Research is being used.

Non-English Speaking Subjects ***(See PPHS policy)***

The consent form and study documents will be translated to Spanish after obtaining IRB approval for the English versions. Clinical Research Coordinators fluent in Spanish will speak to and consent participants in Spanish based on their preferred language.

10. Process to Document Consent in Writing:

The team will adhere to "SOP-HRP-090 Informed Consent Process" and "SOP-HRP-091 Written Documentation of Informed Consent

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11. Vulnerable Populations:

a) Unless already detailed in the protocol, please indicate which of the following populations are either included or excluded in this project: Indicate specifically whether you will include (target) or exclude each of the following populations:

Include	Exclude	Vulnerable Population Type
	X	Adults unable to consent
	X	Individuals who are not yet adults (e.g. infants, children, teenagers)

	X	Wards of the State (e.g. foster children)
	X	Pregnant women
	X	Prisoners

b) Describe other aspects of the subject population that may increase their vulnerability (marginalized populations, poverty, illiteracy and under-education, legal status, home/institution-bound individuals; students participating in their professor's research, cognitively-impaired minors, etc.). For those subjects at an increased risk of not understanding the aims, procedures, risks and benefits of this project, OR whom may be at increased vulnerability to coercion or undue influence, describe additional safeguards included to protect their rights and welfare.

i. We will consent economically or educationally disadvantaged people into the study which reflects the population served by the institution. Those unable to consent will not be included.

c) What steps are being taken to assure that a diverse group of research subjects are approached to participate in this study? What are the projected demographics of the enrolled subjects at study completion.

i. MSH is the largest provider of inpatient and outpatient services in East Harlem. East Harlem (also known as "Spanish Harlem") is located in Northern Manhattan and contains a population of approximately 110,000 people who are primarily low income minorities. The communities surrounding the MMC and JMC site similarly contain a mixed population of Caucasian, African-American, and Hispanic-Americans. Based on the demographics of the communities served by these hospitals and the characteristics of our prior clinic-based studies, we expect that women will comprise approximately 70% of enrolled subjects, Hispanics approximately 40% to 45%, and Black, non-Hispanic 30% to 40%. The proportion of women and minorities in this population is in accordance with the epidemiology of asthma in these communities.

12. Multi-Site Human Research:

a) Besides research sites within the Mount Sinai System please detail the PI's responsibilities for other sites, or overall responsibility for the project?

- Drs. Wisnivesky, Busse and Feldman will be responsible for the oversight and coordination of the entire study. More specifically, Drs. Wisnivesky and Busse will oversee subject

recruitment and data collection at the Mount Sinai site. They will supervise a project manager, a data analyst, and the research assistants. Dr. Wisnivesky will be the contact PI and responsible for all communication with NIH. Given his background in biostatistics, he will also be responsible for the centralized data management at Mount Sinai Hospital. Dr. Feldman will oversee the research assistants and the study activities at both Montefiore Medical Center-Albert Einstein College of Medicine and Jacobi Medical Center sites.

b) If coordinating center functions are taking place at Sinai, whether or not it is also a clinical site, please answer the following with appropriate justification and documentation, if needed:

(i) Are the management, data analysis, and Data Safety and Monitoring (DSM) systems adequate, given the nature of the research involved? Yes

(ii) Is the sample protocols and informed consent documents developed and distributed to each collaborating institution? Yes

(iii) Does each collaborating institution hold an applicable OHRP-approved Assurance? Yes

(iv)Will each protocol be reviewed and approved by the IRB at the collaborating institution prior to the enrollment of subjects? Yes

(v) Have all substantive modifications by the collaborating institution to the sample consent, especially related to risks or alternative procedures, been appropriately justified? Yes

(vi) Will informed consent be obtained from each subject in compliance with HHS regulations? Yes

If this is a multi-site study where you are the lead investigator, describe the management of information (e.g., results, new information, unanticipated problems involving risk to subjects or others, or protocol modifications) among sites to protect subjects.

The PIs will participate in bi-weekly meetings before data collection begins to discuss logistical issues, refinement of survey questions, and any other issues pertaining to the study. During the stage of data collection, each PI will conduct weekly research team meetings at each respective site to assess the status of all aspects of study administration and data collection. Research meetings between both sites will take place bi-weekly, and more often as-needed. The PIs will communicate with each other on a weekly basis by phone, email, or in person. The close proximity of Mount Sinai School of Medicine and Albert Einstein College of Medicine in New York City will allow for frequent in-person

communication.

c) Community-Based Participatory Research

N/A

13. Sharing of individual and study Results with Subjects:

Results will not be communicated with study participants as part of the study is not to influence decision making.

14. External IRB Review History

N/A

15. Control of Drugs, Biologics, or Devices:

N/A