Cover Page

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Study Title: Motivational Interviewing and Air Cleaners for Smokers With COPD (MOVE COPD)

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MOVE COPD Study Protocol

Objectives

Specific Aim #1: To determine whether a multi-component environmental intervention to improve home air quality (PM, SHS and NO2 reduction) will improve respiratory morbidity (i.e., symptoms, quality of life, lung function and reduce risk of exacerbations) in smokers with COPD.

Specific Aim #2: To determine whether a multi-component environmental intervention to improve home air quality (PM, SHS and NO2 reduction) will be associated with intermediate outcome measures known to be linked with long term outcomes in COPD, including airway (induced sputum) and systemic (serum and urine) markers of inflammation and oxidative stress, in smokers with COPD.

Study Procedures

1. **Study design, including the sequence and timing of study procedures.**

We will recruit current smokers (n=150) with moderate to severe COPD and those still smoking after a one-month smoking cessation run-in period will be randomized (estimated 80% of original sample, goal n=120) to receive either 1) air cleaner (with HEPA filters for reduction of PM) and MI for SHS reduction or 2) sham air cleaners. All eligible participants will be offered smoking cessation counseling throughout the study period and will have air monitoring and outcomes assessed at randomization, and 3 and 6-months post intervention. All patients enrolled in this study will continue to have their usual care for COPD as determined by their primary care provider or their usual COPD caregiver. No treatments will be discontinued.

2. Screening Assessment Visit

The initial clinic visit will take place at the Johns Hopkins Asthma and Allergy Center. During the initial clinic visit participant eligibility will be established and informed consent obtained. The screening assessment visit is expected to take approximately 2 hours.
The screening assessment visit will include the following:

- Informed consent
- Pre- and Post-BD spirometry
- Eligibility assessment questionnaires
- Clinical Examination to include anthropometry, vitals and skinfold assessment

3. **Home Air Quality Screening Assessment (IF APPLICABLE)**

In addition, we will have a home air quality screening assessment visit prior to enrollment in the home of participants who have a "home smoking ban" in order to ensure that we randomize homes that have elevated PM values that are more likely to benefit from the intervention of air cleaners to improve indoor air quality. To determine further eligibility, we will place an air pollution monitor in the home (room where the participant reports spending most of his/her time) up to 7 days to measure the air quality. Only participants residing in homes with PM2.5 values ≥ 10 µg /m3 (National Ambient Air Quality Standards (NAAQS) set by the EPA for annual ambient PM2.5 and slightly above WHO standards of 10 µg /m3 for annual indoor PM2.5) will be included. In the case, where we register MIE values borderlines 8-10, we will repeat the MIE assessment only if the participant agree. We will continue to not require home monitoring for homes where smoking is allowed indoors given that PM levels will likely to be elevated.

4. **Run-In Period (1 month)**
All enrolled will be given **two** Motivational Interviewing sessions for smoking cessation during the run-in period. Participants will receive 1 in-person session and 1 phone call session. Nicotine replacement therapy (NRT) will be offered during this period to all participants following approval by a study physician (a pulmonary attending or fellow). Referrals to community resources for additional support will also be provided.

Individuals who quit smoking during the 1 month run-in (self-report 7 day abstinence) will not be randomized nor included in intent-to-treat analyses to maintain adequate power to determine whether pollutant reduction in those who actively smoke provides health benefit. However, if participant would like to continue receiving smoking cessation counseling and NRT they will be referred to the community resources provided during the Motivational Interviewing session. No additional clinic and home visits will be done. An active air cleaner will be offered to ensure there is no incentive to continue smoking and to optimize continued smoking abstinence.

Individuals who continue to smoke (self-report) at the conclusion of the run-in period will be randomized.

5. **Home Visits: Exposure Assessment Methods**

Over the course of the enrollment period, we will assess each subject for 3 seven-day periods (at randomization, 3 months and 6 months post-intervention) to assure that each subject is examined in different seasons; and to evaluate the immediate as well as longer term effects of the interventions on air quality and COPD health. This approach is based on the measurement approach that we have previously demonstrated for PM reduction trials. Indoor air quality monitoring will be conducted over a 7-day period in the room where the participant is expected to spend the most time over the monitoring period.

During each home visit:
1) Monitors for air samples will be set up in the bedroom and in the room in which the participant spends most of his/her time.
2) Detailed questionnaire about home characteristics will be administered
3) A home inspection will be performed
4) Participants will be instructed on how to complete a Time Activity Diary (TAD) and symptom diary which is to be done during the time of the air monitoring period,
5) Outdoor air monitors will be placed in a convenient and secured location outside of each home
6) Dust collection in the main living area and bedroom at home.

The home visits will include the following:
- Environmental monitoring equipment set up and dust collection.
- Instructions on activity diary (TAD), symptom diary (BCSS)

Participant responsibilities:
- Activity diary (TAD daily)
- Breathlessness, Cough and Sputum Scale (BCSS daily)
- Dust collection

Household Inspection: At the time that monitoring is initiated, a trained home inspector will conduct a household inspection which will include the type, salient features and condition of the house including 1) type of home (detached, duplex, row house, apartment) and size of home; 2) type of

furnace (gas, oil, heat pump) as well as heating (radiator, forced air, electric space heater, other); 3) the presence of central or room air conditioning; dehumidifiers, or humidifiers, 4) evidence of cigarette smoke/smell of cigarettes/ashtrays. The home inspection will focus on the living/family room, the kitchen, basement, and the participant's bedroom and identify potential sources of PM, SHS and NO2 as potential confounders to the effectiveness of home interventions.

Collect Dust samples: Study team member will vacuum settled dust samples from the room in which air pollution monitors have been placed to study allergens at home.

Time Activity Diary (TAD): Participants will be asked to keep a simple TAD during each week of sampling. TAD will collect information on participant location (indoor/outdoor/in vehicle, home/work/other), and indoor activities which are gas and particle generating such as cooking, heating, smoking, burning incense or candles. We will adapt TADs previously designed and used for our previous air pollution exposure assessments.

Indoor Air Monitoring: Will be conducted for assessing:
Airborne PM2.5 fine and PM2.5-10- coarse, conducting gravimetric analysis using time-integrated filter based sampler or using a commercially-available low cost PM sensor.
Temperature and Humidity are also monitored.
Ultrafine Particles (UFP) will be measured at high temporal resolution using a Partector (CH Technologies). This device measures lung deposited surface area, which is dominated by particles with diameter less than 100 nm.
Airborne NO2 will be measured with passive samplers (Ogawa badges) using standard methods. Temperature and humidity will also be recorded to adjust NO2 analytical results. All NO2 samples will include 10% blanks and duplicates and will be blank corrected. NO2 samples will be analyzed spectrophotometrically.
Airborne nicotine will be monitored using passive sampling badges according to standard methods. Nicotine is collected by passive diffusion onto glass fiber filter treated with 4% sodium bisulfate solution. The cassette is then sealed and transported back to the laboratory for extraction and analysis using GC-MS, Shimadzu GC-17A, QP 5000, (Shimadzu Corporation, Japan).

Outdoor Air Monitoring: Will be conducted for $PM_{2.5}$ and NO_2 with similar methods as described above for indoor monitoring. Monitors will be placed in a convenient and secured location outside of homes to measure air quality. The monitoring machines will run day and night during each of the 3 periods of seven days of monitoring. While they run, they make no more noise than a pump in a fish tank. We will give you the results of the air quality test after the study is completed

± *We will provide participants the results of the air quality test after the study is completed.*
**** If the participant is unable to attend their clinic visit, questionnaires and data collection may occur at home and/or by phone with the exception of six-minute walk and albuterol administration for spirometry.*

6. **Clinical Visits: Outcomes Assessment**

Outcomes will be assessed at the end of each monitoring period (except exacerbations and health care utilization outcomes, which will be assessed by monthly telephone calls). The outpatient visits will take place in the pulmonary clinic at the Johns Hopkins Bayview Asthma and Allergy Center.

The clinical visit will include the following:

- Assessment of general health status and questionnaire about sociodemographic variables (age, gender, race/ethnicity; family history of lung disease).
- Assessment of a validated food questionnaire to analyze diet patterns.
- Completion of respiratory and general health questionnaires: Quality of Life (QOL) will be determined using the St. George's Respiratory Questionnaire (SGRQ), Modified Medical Research Council Dyspnea Scale (MMRC), University of California San Diego Shortness-of-Breath Questionnaire (UCSD SOBQ), COPD Assessment Test (CAT), modified-American Thoracic Society and Division of Lung Diseases of the National Heart and Lung Institute Questionnaire (ATS-DLD-78 adult), Berlin Sleep questionnaire, Pittsburgh sleep quality index. Hospital anxiety and depression scale, perceived stress 10-items and hardship questionnaire.
- Lifestyles questionnaires: electronic cigarette, marijuana and alcohol intake (FAST)
- Adverse Childhood Experience (ACE)
- Everyday Discrimination Scale (EDS)
- Cognitive Impairment Tests (MoCA-Test)
- Social Cognitive measures: For each SCT construct, participants will be asked to rate how much confidence, importance, and motivation they had to implement a home smoking ban or quit smoking on a 10-point scale, where 1 is "not at all sure, not at all important, don't want to do it at all", 10 is "completely sure, extremely important, really want to do it every day", and 5 is "somewhere in between". We will also administer our previously validated measure of SHS positive and negative expectancies and knowledge of SHSe harm, which has been shown to be associated with SHS air nicotine levels.
- COVID-19 impact on health questionnaires (long version and short follow up): to assess exposure to COVID-19, experiences with testing, taking precautions with masking and isolating, and about impacts of the pandemic on well-being.
- Nicotine dependence will be measured using the Fagerstrom Test for Nicotine Dependence which is a standard instrument for assessing intensity of physical addiction to nicotine.
- Clinical Examination to include anthropometry, vitals and skinfold assessment
- Breathing Tests: Spirometry will carry out to measure lung function. We will obtain at least three acceptable and reproducible spirometric maneuvers from a maximum of eight in accordance to the American Thoracic Society (ATS) and European Respiratory Society guidelines.
- Salivary cotinine will be assessed during each clinic visit to assess smoking status.
- Six Minute Walk Test will be assessed during each clinic visit to test participants exercise tolerance. Participant will be asked to walk for 6 minutes of a flat surface to see how far can go. If participants use oxygen when walking, they will use it for this test. As a safety precaution, the amount of oxygen in their blood will be measured using a pulse oximeter, which is a small device that attaches to the index finger.
- Blood Draw: Fasting blood sample will be collected to measure systemic markers of inflammation and oxidation, and it will include a complete blood count with differential (CBC with diff) to assess effects of pollution and air cleaners on inflammatory profile.

7. Telephone Calls

01 call (during the 1 month run-in period) for Motivational Interviewing for smoking cessation: All participants will receive 1 call for smoking cessation prior to randomization. *Additional counseling sessions will be scheduled for any participant or family member(s) interested in smoking cessation during this period.*

04 calls (between randomization and the 3 month-follow-up) for Motivational Interviewing for home/car smoking ban (HCSB): The MI-component of the intervention will be adapted from the PRIDE phone-based MI intervention and delivered by a health coach. Each participant will receive 4 phone sessions between baseline and the 3 month visit focused on implementing a home smoking ban. All participants regardless of randomization group will receive the 4 phone call sessions (between baseline and the 3 month clinic visit) focused on smoking cessation counseling. Only participants randomized to the active group will receive the additional Motivational Interviewing for HCSB during the calls.

04 Monthly calls (from randomization to 6 month-follow up) to assess Exacerbations and Health Care Utilization: Information on unscheduled doctor visits, emergency room visits, and days hospitalized, and intensive care unit admissions will be collected at each visit from all participants and by monthly telephone calls.

03 Monthly Follow up calls (after final home visit) Individuals will also be contacted monthly for 3 months after the final home visit by study coordinators, in order to ascertain whether exacerbation events were experienced by participants. The Telephone Exacerbation questionnaire that will be administered, will take about 5 minutes.

8. Study duration and number of study visits required of research participants.

The study duration is 5 years and each subject will be enrolled for 9 months. There will be one screening assessment visit and one home air quality assessment visit (if applicable) prior to enrollment, 1 month of run-in period (including two MI sessions) and 3 home monitoring visits preceding 3 follow-up clinical visits.

9. Justification for inclusion of a placebo or non-treatment group.

Randomization: At the conclusion of the run-in period, subjects enrolled will be randomly assigned to one of two treatment arms: 1) active air cleaners and MI for SHS reduction (n=60) and 2) placement of sham air cleaners and continued smoking cessation counseling (n=60). Randomization will be stratified by season and will be performed by block to assure equal sized populations in each arm. This strategy also will ensure that each group is balanced with respect to season of randomization.

10. Treatment Groups.

1) **Active Treatment arm:** The active treatment arm will receive two active air cleaners with HEPA filters as well as 4 sessions of phone based motivational interviewing to support a home smoking ban and SHS reduction (in addition to the smoking cessation counseling received by all study participants).

Rationale: Two air cleaners will be deployed in the home to be consistent with our previous trials that have successfully reduced PM and improved respiratory morbidity. Air cleaners will have HEPA filters which remove PM. As portable air cleaners have not shown efficacy in reducing SHS exposure this intervention also targets a home smoking ban for both SHS and PM reduction, in order to provide greatest reduction in pollutant exposure and maximize ability to show that air quality improvement can improve health in smokers.

Active air cleaner: Air cleaners containing HEPA and capable of removing PM filter will be placed in the bedroom and room where the participant reports spending the most time. Air cleaners are

suitably sized to provide clean air delivery rates for the rooms in which they will be placed. Participants will be instructed to run the air cleaners continually during the course of the study. Filtering elements will be maintained and changed based on manufacturer's instructions by study staff. Data logging current meters will be used to determine the total time of air cleaner use. The meters, inserted inside the air cleaner to avoid tampering, sense the change in electric current associated with turning the air cleaners on /off and record the time/date for each on/off event. Families will be informed that air cleaner use is monitored.

Motivational Interviewing for home/car smoking ban (HCSB): The MI-component of the intervention will be adapted from the PRIDE phone-based MI intervention and delivered by a health coach. Each participant will receive 4 phone sessions between baseline and the 3 month visit focused on implementing a home smoking ban and additional counseling sessions will be scheduled for any participant or family member(s) interested in smoking cessation. Participants will be paid $25 for completing all four sessions to ensure completion. These incentives are provided regardless of behavior change and are included in this efficacy study to evaluate whether a full dose of intervention results in meaningful changes in behavior.

2) **Control Arm:** the Control arm will receive sham air cleaners and continued counseling for smoking cessation. A control arm is needed to ensure that reduced pollutant levels and health effects are not due to temporal trends and 'placebo effects' of being enrolled in an intervention trial.

Sham Air Cleaner. Homes in the control group will receive sham air cleaners that have the internal HEPA filters removed, but which will run normally, including similar noise, airflow and overall appearance compared to active air cleaners, thus blinding participants to filter status. We will use tamper-proof fasteners to replace conventional screws to prevent tampering with the air cleaner or opening by participants to learn if filters are in place. In our previous studies, compliance with active and sham air cleaners have been similar suggesting adequate blinding to the sham. At the end of the study, all participants will receive active air cleaners.

Smoking Cessation counseling and Nicotine Replacement Therapy (NRT): Smoking Cessation counseling will be offered to all eligible participants throughout the study. Study will offer NRT to all participants during the Run-In period. If participants would like to continue NRT after the Run-In period they will be referred to the community resources provided during the Motivational Interviewing session.

Participants in the control group will receive 4 sessions of education smoking cessation counseling as an attention control condition. Cognitive based therapy will be provided to participants and will focus on anticipating triggers for relapse and developing coping strategies to deal with withdrawal. Problem solving and skills training will be integrated to support cessation. Participants will be paid $25 for completing all four sessions to ensure completion. These incentives are provided regardless of behavior change and are included in this efficacy study to evaluate whether a full dose of intervention results in meaningful changes in behavior.

11. Definition of treatment failure or participant removal criteria.

Participants may be removed from the study early if they are not living in their home during the study time (including admission to the hospital). In these cases, monitoring of the home environment would not reflect exposure.

12. **Description of what happens to participants receiving therapy when study ends or if a participant's participation in the study ends prematurely**.

At the end of the study, participants in the control group will also receive active air cleaners.

13. Inclusion/Exclusion Criteria

Inclusion Criteria:
1) Age ≥ 40 years,
2) Physician diagnosis of COPD,
3) GOLD Stage II-IV disease with (post-bronchodilator) FEV1/FVC < 70% and FEV1 (% predicted) < 80%. *IF FEV1/FVC <70% and FEV1 (% predicted) ≥ 80%, additional requirement will apply/will be asked: CAT score ≥ 10 OR exacerbation history during the last 12 months. Also, IF available for screening purposes: participant can provide a previous PFT report within the last 6 months.*
4) Tobacco exposure ≥ 10 pack-years, and
5) Current smoker with an eCO ≥ 7 ppm to confirm smoking status (Deveci Erhan S., et al, 2004). We will employ a combination of self-report and a biochemical marker to identify former-smokers. Exhaled CO (eCO) and salivary cotinine will be used as a marker of smoking status, as they are easy to perform, provides immediate data and is non-invasive (*If no eCO performed due to COVID-19 pandemic safety reasons, we will rely on self-report smoking status and self-report 7-day abstinence questionnaire answers).*
6) No home smoking ban. *IF smoking is not allowed indoor (inside participant's home) then a "home air quality assessment visit" will be done. MIE PM ≥ 10 mcg/m3 at home air quality assessment visit will apply for enrollment (see also 4.a.2). In the case, where we register MIE values borderlines (8-10), we will repeat the MIE assessment if the participant agree.*

Exclusion criteria for all participants will include:
1) Chronic systemic corticosteroids, equivalent to > 10 mg of daily prednisone continuously for ≥ 3 months in the past 12 months,
2) Other chronic lung disease, except those with history of asthma if it felt by the investigator not to be a primary diagnosis.
3) Living in location other than home (e.g., long term care facility) and
4) Home owner or home occupant planning to move or change residence within the study period.
5) Air Cleaners drop off (home visits temporary criteria due to COVID-19): if participant is unable to bring air cleaners inside the home and setting them up or if no one else living in the home can help, the baseline visit will be rescheduled or cancel to a later time.