IRB NUMBER: 12-10510
IRB APPROVAL DATE: 01/14/2021
IRB EXPIRATION DATE: 01/13/2022

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title:

Lung physiologic, radiographic, and inflammatory changes due to secondhand tobacco smoke

This is a medical research study investigating the physiologic, radiographic, and inflammatory responses of lungs to chronic exposure to secondhand tobacco smoke. Your study investigator, Mehrdad Arjomandi, MD, or his associates from University of California San Francisco will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about participating. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your study investigator.

Why is this study being done?

Over the past several decades, large portions of the U.S. population have experienced longstanding exposure to secondhand tobacco smoke (SHS) at home and work; however, the health effects and functional consequences of chronic exposure to SHS on lungs are unknown. As this population who has endured the greatest exposure to SHS ages, it has become increasingly important to better understand the resulting lung damage caused by their longstanding SHS exposure. In this research plan, the investigators propose to study a population of nonsmoking people who have been exposed to heavy secondhand tobacco smoke through their work environment, such as flight attendants who worked in commercial aircraft prior to the ban on cigarette smoking and casino workers who worked for extended hours in casinos where smoking was or is allowed, to examine the lung damage and functional consequences of chronic exposure to SHS. In addition, healthy nonsmoking people with no history of exposure to SHS, such as flight attendants who worked for airlines after smoking ban was put in place, will be recruited as control population for comparison with those who have been exposed to SHS.

Additionally, because it is unclear how secondhand smoke exposure may affect a person's response to COVID-19 illness, we are planning to obtain additional information and blood samples that would help determine the likelihood of people with secondhand smoke exposure to develop severe disease with COVID-19.

Who is sponsoring this study?

This research is funded by the Flight Attendants Medical Research Institute (FAMRI) and by the UCSF Cardiovascular Research Institute (CVRI). The investigators do not have a direct financial interest in the final results of the study. This disclosure is made so that you can decide if any financial relationship will affect your willingness to participate in this study.

How many people will take part in this study?

A total of 225 people will take part in this study.

What will happen if I take part in this research study?

Event	Description	Time
Pre-consent Home Procedures		
Study introduction	If you are interested in the study, a member of our research team will explain the details of the study to you over the phone. You are encouraged to ask questions about the study at this time.	30 minutes
Consent form	You will be mailed a copy of the consent form, which you will read at home. If you have questions or would like to discuss any part of the study, you may contact the study personnel at any time by phone or can ask them in person when you come to UCSF or SF VAMC for your first visit.	30 minutes
Questionnaires	You will fill out five questionnaires about your exposure to SHS and other pollutants, your health and quality of life, and your physical fitness.	30 minutes
Baseline Visit (Visit 1)		
Consent	Upon your arrival to Visit 1, you will have the opportunity to ask any questions or review any portions of the consent document. After your questions are answered, you will sign the consent document.	15 minutes
Physical Exam and Interview	You will also be asked questions about your health status to establish your eligibility for the study. In addition, you will undergo a limited physical examination including a brief physical exam and the measurement of your vital signs (blood pressure). The exam will also include a baseline electrocardiogram. The physical exam and interview will be similar to those done for regular medical care.	15 minutes
Breathing Test (Pulmonary Function Test)	You will be asked to perform baseline breathing tests at rest (pulmonary function test or PFT). These tests evaluate lung function at rest. A finger stick may be required to obtain a sample of blood (1/4 teaspoonful) to measure hemoglobin and carboxyhemoglobin levels. **You may be asked to complete this procedure on a separate additional visit.*	60 minutes

Maximum Effort Exercise Testing	You will be asked to perform a progressive incremental exercise increased by 10-30 watts per stage to symptom limitation. During this test, you will sit on a stationary bicycle and pedal with your legs while an electrocardiogram is recorded. Vital signs (blood pressure, oxygen pulse, and respiratory rate) will also be measured at each work rate. In addition, tiny samples will be taken automatically of the gas you breathe out in order to measure the amount of oxygen you consume during exercise. You will be asked to exercise as long as you can. Exercise will be stopped when you become too tired; if you experience any problems such as chest pain, shortness of breath; or abnormal heart rhythm; or if you ask to stop exercising for some other reason. You will rest for 30 minutes before the next procedure. A finger stick may be required to obtain a sample of blood (1/4 teaspoonful) to measure hemoglobin and carboxyhemoglobin levels.	90 minutes
Inspiratory Capacity Exercise Testing	You will be asked to perform a series of breathing tests with exercise. You will exercise again at a low (20%), medium (40%), medium-high (60%), and high (80%) workload (based on the prior exercise test). During this exercise test you will be asked to perform breathing tests as described above at each workload, while you continue to exercise on a stationary bicycle. While you are exercising, you will wear nose clips and breathe through a mouthpiece so that the study doctor and his associates can measure the size of each breath and the rate at which you breathe.	45 minutes
CT Scan (optional)	If you have a history of heavy exposure to SHS, you may be asked to undergo two computer tomography tests (also known as CT scans) of the chest, one scan at maximum inspiration and one scan at maximum expiration. ACT scan uses special x-ray equipment to make detailed pictures of body tissues and organs. For the CT scan, you will need to lie still on a table with your arms above your head inside a large doughnut-shaped machine. The table will move and the machine will make clicking and whirring noises as the pictures are taken. If you have never worked as a flight attendant, or flew as a flight attendant only after cabin smoking was banned, you will not participate in the CT Scan.	30 minutes
Genetic Testing	The donated samples will be tested for polymorphism in genes associated with response to oxidative injury as it occurs with inhalation of tobacco smoke. Although we will use the specimens for genetic research, we will not put the results in your medical records. The research will not change the care you receive. Your specimens and any information about them will be kept until it is used up or destroyed. It may be used to develop new drugs, tests,	--

	treatments or products. In some instances, these may have potential commercial value. Your personal health information cannot be used for additional research without additional approval from either you or a review committee.	
Home Procedures #1		
Albuterol or Placebo Inhalation	You will be using a metered dose inhaler containing either a bronchodilator (albuterol) or a placebo metered dose inhaler (2 puffs equivalent to 180 mcg twice a day) for 4 weeks.	60 minutes
Measurement of Daily Physical Activity using an Accelerometer	During your 4th week of using albuterol or a placebo inhaler, you will be asked to wear an accelerometer to measure your usual level of daily activity during the day for a period of one week. It is crucial that you wear the monitor regularly for 5 consecutive days for at least 8 hours a day. At the end of the week, you will be returning it in a prepaid pre-addressed envelope so we can extract and analyze the data from it. This will enable us to determine whether Albuterol can improve your daily physical activity.	10 minutes
Week 1 Check-in Call	To ensure safety, one week after the initiation of albuterol or placebo inhaler a research coordinator will give you a call and ask if you are experiencing any symptoms. If there is any concern, then the study investigator might contact you again for further evaluation and planning.	15 minutes
Questionnaires	After 4 weeks of using albuterol (or placebo) inhaler, you will again complete two questionnaires about your health and quality of life that you will mail in a pre-paid pre-addressed envelope.	10 minutes
Visit 2		
Physical Exam and Interview	You will be asked questions about your health status to confirm your eligibility for the study. In addition, you will undergo a limited physical examination including a brief physical exam and the measurement of your vital signs (blood pressure). The exam will also include a baseline electrocardiogram. The physical exam and interview will be similar to original physical exam and interview that was performed during Visit 1.	15 minutes
Breathing Test (Pulmonary Function Test	You will be asked to perform a repeat breathing test at rest (pulmonary function test or PFT). These tests will evaluate lung function at rest.	30 minutes
Maximum Effort Exercise Testing	you consume during exercise. You will be asked to exercise as long as you can. Exercise will be stopped when you become too tired; if you experience any problems such as chest pain, shortness of breath; or abnormal heart rhythm; or	90 minutes

	if you ask to stop exercising for some other reason. You will rest for 30 minutes before the next procedure. A finger stick may be required to obtain a sample of blood (1/4 teaspoonful) to measure hemoglobin and carboxyhemoglobin levels.	
Inspiratory Capacity Exercise Testing	You will be asked to perform a series of breathing tests with exercise. You will exercise again at a low (20%), medium (40%), medium-high (60%), and high (80%) workload (based on the prior exercise test). During this exercise test you will be asked to perform breathing tests as described above at each workload, while you continue to exercise on a stationary bicycle. While you are exercising, you will wear nose clips and breathe through a mouthpiece so that the study doctor and his associates can measure the size of each breath and the rate at which you breathe.	45 minutes
Sputum Induction (optional)	You may be asked to donate a sputum sample by undergoing sputum induction. During this procedure, you will inhale salty water (3% saline) mist produced by an ultrasonic nebulizer for 20 min. You will be asked to cough periodically (every 2 minutes) throughout the procedure, and place the produced sputum sample in a sterile container.	60 minutes
Home Procedures #2		
Albuterol or Placebo Inhalation	You will be using the alternate inhaler that you did receive during Home Procedure #1 (a metered dose inhaler containing either albuterol or a placebo metered dose inhaler) (2 puffs equivalent to 180 mcg twice a day) for 4 weeks.	60 minutes
Measurement of Daily Physical Activity using an Accelerometer	During your 4th week of using albuterol or a placebo inhaler, you will be asked to wear an accelerometer to measure your usual level of daily activity during the day for a period of one week. It is crucial that you wear the monitor regularly for 5 consecutive days for at least 8 hours a day. At the end of the week, you will be returning it in a prepaid pre-addressed envelope so we can extract and analyze the data from it. This will enable us to determine whether Albuterol can improve your daily physical activity.	10 minutes
Week 1 Check-in Call	To ensure safety, one week after the initiation of albuterol or placebo inhaler a research coordinator will give you a call and ask if you are experiencing any symptoms. If there is any concern, then the study investigator might contact you again for further evaluation and planning.	15 minutes

Questionnaires	After 4 weeks of using albuterol (or placebo) inhaler, you will again complete two questionnaires about your health and quality of life that you will mail in a pre-paid pre-addressed envelope.	10 minutes
Washout Period	There will be a minimum of two weeks between the completion of the accelerometer and the Visit 2 date to allow the administrated treatment (albuterol or placebo) to be eliminated from the body.	--
Visit 3		
Physical Exam and Interview	You will be asked questions about your health status to confirm your eligibility for the study. In addition, you will undergo a limited physical examination including a brief physical exam and the measurement of your vital signs (blood pressure). The exam will also include a baseline electrocardiogram. The physical exam and interview will be similar to original physical exam and interview that was performed during Visit 1.	15 minutes
Breathing Test (Pulmonary Function Test	You will be asked to perform a repeat breathing test at rest (pulmonary function test or PFT). These tests will evaluate lung function at rest.	30 minutes
Maximum Effort Exercise Testing	You will be asked to perform a progressive incremental exercise increased by 10-30 watts per stage to symptom limitation. During this test, you will sit on a stationary bicycle and pedal with your legs while an electrocardiogram is recorded. Vital signs (blood pressure, oxygen pulse, and respiratory rate) will also be measured at each work rate. In addition, tiny samples will be taken automatically of the gas you breathe out in order to measure the amount of oxygen you consume during exercise. You will be asked to exercise as long as you can. Exercise will be stopped when you become too tired; if you experience any problems such as chest pain, shortness of breath; or abnormal heart rhythm; or if you ask to stop exercising for some other reason. You will rest for 30 minutes before the next procedure. A finger stick may be required to obtain a sample of blood (1/4 teaspoonful) to measure hemoglobin and carboxyhemoglobin levels.	90 minutes
Inspiratory Capacity Exercise Testing	You will be asked to perform a series of breathing tests with exercise. You will exercise again at a low (20%), medium (40%), medium-high (60%), and high (80%) workload (based on the prior exercise test). During this exercise test you will be asked to perform breathing tests as described above at each workload, while you continue to exercise on a stationary bicycle. While you are exercising, you will wear nose clips and breathe	45 minutes

	through a mouthpiece so that the study doctor and his associates can measure the size of each breath and the rate at which you breathe.	
Blood Draw	You will be asked to give a blood sample for laboratory tests. Approximately up to 3 tablespoons of blood will be drawn by inserting a needle into a vein in your arm for these tests.	5 minutes
Visit 4		
Follow up Longitudinal Study	You may also be asked to participate in a follow up study with resting breathing test 5 years from your original participation in the study. During this follow up study, you will be asked to complete a set of heath questionnaires (same as above), and then undergo resting PFT (same as in above).	120 minutes
Total Time in the Pulmonary Function Lab:	***11.25 hours***	
Total Time for at Home Procedures:	***5 hours***	
	Total Time:	***18 – 18.5 hours***

Additional Optional COVID-19 Visit: If you agree to participate in the optional additional COVID-19 procedures, we will contact you for the following:

1- Re-consent: The original consent form you signed is still valid. However, if you agree to participate in the additional COVID-19 visit, we would like you to sign this revised consent form that reflects these changes. This will take about 15 to 30 minutes.

2- Questionnaire: We will administer a specific COVID-19 questionnaire via mail or over the phone. The questionnaire takes approximately 5 to 30 minutes.

3- Blood draw: We will ask you to come into the medical center for a blood draw and donate two tablespoons (30 mL) of blood. This will take up to 30 minutes.

Your blood will be stored to be tested for COVID-19 antibodies at a later time. We may or may not share the result of the blood test with you depending on a number of factors.

When you are finished performing the tasks in the main part of the study (Visit 1 and the at-home procedures) ...

- **Results of the Study:** One of the study investigators will review the results of your tests with you in person or by telephone, depending on which is more convenient for you. These results will remain confidential. The results will only be disclosed to your own doctors at your request.

Study location: All study procedures will be done at either the San Francisco VA Medical Center or the UCSF Medical Center.

COVID-19 Precautions: To ensure safety and minimize the risk of COVID-19 infection, you will be asked a safety COVID-19 screening questionnaire. This questionnaire will be administered twice: one day before the scheduled in-person visit and on the day of scheduled

in-person visit. If there is any concern for infection with COVID-19, the visit will have to be rescheduled after the participant is symptom free for at least 6 weeks.
You will be asked to undergo COVID-19 testing 48 to 72 hours prior to scheduled study visit. The COVID-19 test involves placing a swab in the back of your nose or mouth to collect cells and secretions. The swab will be sent to the laboratory for testing to see if you are infected with the coronavirus that causes COVID-19. If the result of the COVID-19 test is positive, you should seek follow-up clinical care with your own provider outside of the research study. The study visits will also be rescheduled until after a repeat COVID-19 test is negative. COVID-19 testing is being performed strictly as a clinically required safety measure and not as part of research testing. According to California regulations all COVID-19 test results (positive, negative or inconclusive) will be reported to the county public health department.

The breathing and exercise tests that will be performed as a part of this study generate aerosolized respiratory secretions in the form of droplets from coughing, sneezing, and/or breathing heavily. As such, this testing does pose a considerable risk for the spread of infection to the study staff and surrounding surfaces within and around the testing areas, even in asymptomatic patients.

Study staff will perform each visit in accordance with the University of California, San Francisco safety guidelines.

- All study staff will wear appropriate Personal Protective Equipment (PPE), including face shields, N95 masks and gloves. We will ask that all participants wear surgical masks when entering facility and during visit.
- Study staff will make an effort to physical distance as much as possible throughout the visit.
- Study staff will take extra care to sanitize all work station surfaces and equipment.

How long will I be in the study?

Participation in the main part of the study will take a total of about 11.25 hours over a minimum of 10 weeks. During this period, you will conduct about 1.5 hours worth of the study at home, and 4.25 hours worth of the study during the baseline visit to the UCSF Medical Center or SF VAMC, and 1.5 hours worth of the study by completing the first at home procedures. The second visit to the UCSF Medical Center or SF VAMC will be worth 4 hours, and the second set of at home procedure will be 1.5 hours. The third visit to the UCSF Medical Center or SF VAMC will be worth 3 hours. After 3-5 years, you will be asked to participate in a follow up portion of the study, which will require you to come to the UCSF Medical Center or SF VAMC for a visit lasting about 2 hours. The following table summarizes your time commitment in the study: (For a more detailed description of how long each procedure will take, please see the table in the "Procedures" section above.)

Event:	**Time after *enrollment* in the study:**	**Time commitment required:**
Pre-Consent Home Procedures:	Prior to enrollment	1.5 hours
Visit 1 at UCSF campus:	1-2 weeks	4.25 hours
Home Procedures #1: **	2-5 weeks	1.75 hours

Visit 2 at UCSF campus:	5-6 weeks	4 hours
Home Procedures #2: **	6-7 weeks	1.75 hours
Visit 3:	9-10 weeks	3 hours
Visit 4 at UCSF campus:	3-5 years	2 hours
Total:	**3- 5 years**	**~ 18 – 18.5 hours**

**You will be wearing an accelerometer (a sort of pedometer) on your belt or waist during the day for a one-week period before and after your Visit 1. Putting on and removing the accelerometer will take only about a minute or two, and will be done by you in your own home- you will not be asked to come to UCSF or SF VAMC for this part of the study. The accelerator is to be worn during the day for a week, but wearing the accelerometer is done while you are doing your usual daily activities at home and/or work, and will not prevent you from completing any normal activities, or make normal activities take longer than usual.

If you agree to participate in the additional optional COVID-19 procedures, we will contact you for re-consent, specific COVID-19 questionnaire and an additional blood draw which may take an additional **1-1.5 hours**.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop, and they will tell you how to stop your participation safely.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

- **Physical Exam**: The risks associated with physical exam are minimal.
- **Interview**: You may experience some anxiety or discomfort when describing your medical history. If you do not feel comfortable answering a particular question, please let a member of the research team know. In some cases, you may be able to skip that question and still be eligible to participate in the research study. In some other cases, however, it may be critical that the research team know the answer to a particular question before you can complete the study, so that the research team can ensure that you can safely complete the study, and/or that the research questions can be answered. If at any point you feel uncomfortable answering a question, the research team can advise you on which questions can and cannot be skipped.
- **Questionnaires**: You may experience feelings of discomfort and embarrassment in answering some of the questions. If you do not feel comfortable answering a particular question, please let a member of the research team know. In some cases, you may be able to skip that question and still be eligible to participate in the research study. In some other cases, however, it may be critical that the research team know the answer to a particular question before you can complete the study, so that the research team can ensure that you can safely complete the study, and/or that the research questions can be

answered. If at any point you feel uncomfortable answering a question, the research team can advise you on which questions can and cannot be skipped.

- **Blood drawing (venipuncture)** causes temporary bruising and discomfort at the site of needle puncture. Very rarely blood draws can cause fainting. The bruise is usually painless and disappears within a few days. There is a small risk of infection at the site of the blood draw. This would result in tenderness and swelling in the area of the puncture site and possible fever. If this were to occur antibiotics would be administered to treat the infection.
- **Blood Tests:** The tests performed on blood samples do not cause any risks or hazard to you. The results of the blood tests are kept confidential to the limit of law as detailed below.
- **Pulmonary function tests (spirometry)** may cause you to feel short of breath. In rare circumstances, people can faint or feel lightheaded due to breathing hard.
- **Sputum Induction** may cause a salty taste in the mouth, or nausea. It can also provoke moderate bronchoconstriction. If bronchoconstriction does occur during sputum induction, it can be rapidly reversed by treatment with inhaled albuterol.
- **Maximum Effort Exercise Test and Inspiratory Capacity Exercise Test** can cause chest pain, shortness of breath, leg discomfort, or, rarely, abnormal heart rhythms. There is a very small chance, less than one in a thousand, of a heart attack being caused by the stress test. Exercise stress testing could also cause emotional distress, if the results of your test are abnormal.
- **Albuterol Administration:** Albuterol inhaler is a bronchodilator medication typically used for treatment of asthma or COPD, and is delivered via a metered dose inhaler at a very small dose to the lungs where it can affect the airways. Albuterol can cause dizziness, tremors, nervousness, headache, sore throat and/or nausea. These side effects, if occur, are relatively mild, but you should inform the study doctor if they occur and are bothersome. Less commonly, inhalation of albuterol may cause an increase in heart rate or blood pressure in some individuals. However, at doses used in this study, these types of side effects are unlikely, but if they occur, the drug may need to be discontinued.
- **Randomization risks:** In the first part of the study, you will be assigned to one of two treatment programs by chance, either a bronchodilator (albuterol) or placebo metered dose inhaler. In the second part of the study, you will be assigned to the alternate treatment program. The treatment you may receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.
- **Placebo risks:** While you are in the group that receives placebo, your condition will go without the active (study) treatment for 4 weeks. You will be closely monitored to ensure your safety in receiving the placebo treatment.
- **CT scanning** is a non-invasive procedure, but requires administration of a small amount of radiation. This radiation exposure is not necessary for your medical care and is for research purposes only. Although radiation exposure from CT scan may increase the possibility of inducing cancer, this probability is thought to be very small in comparison to background natural radiation. The amount of radiation that you will receive as a result of participating in this study will be approximately equivalent to the yearly natural background of radiation in the US [(measured to be approximately 3 milli-Sievert (mSv)]. If you are pregnant or breast feeding, you SHOULD NOT participate in this study. If you have any questions regarding the use of radiation or the risks involved, please consult the physician conducting the study. Having a CT scan may also cause some added discomfort for you. In particular, you may be bothered by feelings of claustrophobia when placed inside the CT scanner.

  In addition, the findings from CT scan done for research purposes may cause some emotional distress. CT scans produce a very precise picture of the chest and the lungs,

and thus may show small irregularities. Most of the time, these irregularities represent an area of scarring due to old respiratory infection or accumulation of mucus and are with no health consequence; however, these irregularities could also be indicative of a small cancer in the lungs. We will not be able to determine the nature of these irregularities by the CT image alone, and further follow up with repeated imaging or biopsy may be needed to determine the nature of the irregularities. While we do provide a report of your CT scan, we will not perform the follow up of any irregularities that may appear in the scans. You will have to perform your follow up with your primary care physician and/or a lung specialist. You and your physicians will be responsible for further follow up of these irregularities.

Discovery of these irregularities may cause significant stress for you during the period of follow up while repeat CT scans or biopsy are performed, as you may be concerned about the nature of the irregularities in your lungs. We would like you to be aware of this risk and the possible emotional distress that may be associated with it before deciding if you will participate in the research study.

- **COVID19 Testing:** Testing for COVID19 requires a swab from the back of your nose or mouth to test for current infection of the virus. This may cause nasal discomfort, nasal stuffiness and a gag reflex. It may also cause your eyes to tear up temporarily. A nasal swab also has the possibility of causing nasal bleeds, especially in people who have a tendency to bleed. There are several other implications of a positive COVID-19 test:
  - You will need to contact your doctor to arrange for treatment. If you do not have a doctor, the study physician will help you find medical care.
  - You should follow the isolation steps (home quarantine steps) that are recommended by your local Department of Public Health (we will provide you with a copy of the COVID-19 information sheet from the San Francisco Department of Public Health). Because you could have unknowingly infected others with coronavirus, you should also share the COVID-19 information sheet with everyone who you had close contact with in the past 48 hours. These contacts need to follow home quarantine steps as well. It is possible that someone from your local public health department will contact you to perform contact tracing.
  - Being in home quarantine may affect your ability to work, if you work outside your home.
  - A positive COVID-19 test may mean that your children will be asked to stay home from their usual daycare.

- **Measurement of Your Daily Physical Activity using an Accelerometer** may cause you some discomfort or be an inconvenience, but otherwise the risks are minimal.

- **Genetic Testing:** Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health. To further safeguard your privacy, genetic information obtained in this study will not be placed in your medical record. Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. If you do not share information about taking part in this study, you will reduce this risk. Although your name will not be with the sample, it will have other facts about you such as race, age, and sex. These facts are important because they will help us learn if the factors that cause increased response to secondhand smoke are the same or different based on these facts. Thus, it is possible that study finding could one day help people of the same race, age, or sex as you. However, it is also possible through these kinds of studies that genetic traits

might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

- **Reviewing the results of the study** may cause some emotional distress. CT scan produces a very precise picture of the chest and the lungs. Although it is very useful in diagnosing various diseases, it may also show very small irregularities of unknown cause or importance. Sometimes these irregularities have no particular health significance. (For example, it might be an area of scarring due to old respiratory infection, or an old rib fracture.) But sometimes we cannot determine the nature of these irregularities, whether they are benign and can be ignored, or could possibly be malignant and need follow up. In the majority cases, these unknown irregularities end up being benign and of no health consequence.

  When such irregularities are found incidentally on CT scans, the usual recommendation is to follow them by repeated CT scanning over a period of one to two years to see whether the irregularities are disappearing, stable, or growing. Depending on these findings, further work up may be recommended. This may cause significant stress because for a period of one to two years while repeat CT scans are performed, as you may be concerned about the nature of the irregularities in their lungs.

  If such irregularities are found on your CT scan, we will notify you and will ask you to consult your primary care physician on whether these irregularities should be followed or not. While we will provide you the images and their interpretation and will counsel you on any further evaluation needed, the you and your primary care physician will be responsible for further follow up of any such irregularities.

- **Unknown Risks:** There is no experimental treatment in this study and hence there are no unknown risks.

- **Optional COVID-19 Follow-up Visit:** If you participate in the optional COVID-19 Follow-Up Visit, we will draw blood from you. This may cause discomfort associated with inserting the needle. There is also a possibility of bruising at the site, and/or very rare risk of infection. You may also experience dizziness or lightheadedness, all of which are brief. The volume of blood drawn will be limited to 2 tablespoons and does not involve any other significant risk or discomfort.

Ask your study investigator if you would like to have more information about any risks and side effects of this study.

Who is eligible to participate?

You are being asked to participate in this study because (a) you have been exposed to secondhand tobacco smoke, OR (b) you agree to volunteer as a healthy ("control") subject.

Who should not participate in this study?

Those who have a:

- History of active tobacco use of over 1 pack-year of cigarettes in their lifetime.
- History of active cardiac disease, uncontrolled hypertension, congestive heart failure.
- History of respiratory diseases such as asthma, emphysema, chronic bronchitis, and sarcoidosis.

- Debilitating chronic illnesses such as severe lupus or rheumatoid arthritis.
- Physical inability to perform exercise testing.

Are there benefits to taking part in the study?

If you are in the group that receives albuterol administration and it proves to treat your condition more effectively than without taking any medications, you may benefit from participating in the study, but this cannot be guaranteed. The investigators hope that knowledge gained from this study will provide important information about the health effects of exposure to secondhand tobacco smoke. Future patients and their physicians may benefit from this study due to improved understanding of the effects of secondhand smoke. In addition, findings from this study may contribute to public policy decisions to further limit smoking in public areas in the future.

Additionally, it is unclear how secondhand smoke exposure may affect a person's response to COVID-19 illness. Secondhand smoke exposure may affect the severity of COVID-19 illness, and thus learning its interaction should be helpful in how COVID-19 should be managed.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Not participating in this study
- Participating in a different research study

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record is kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The Flight Attendants Medical Research Institute
- The University of California
- The National Cancer Institute (NCI) and other government agencies, e.g., the Food and Drug Administration (FDA), involved in keeping research safe for people.

Participation in research may involve a loss of privacy, but information about you will be handled as confidentially as possible. A medical record will be created because of your participation in this study. Your consent form and some of your research test results will be included in this record. Therefore, your other health care providers may see your test results and become aware of your participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

A medical record will be created because of your participation in this study. Your scans will be included in this record. Therefore, health care providers with access to medical records may become aware of the results of your scan. Hospital rules require that all health care providers treat information in medical records confidentially.

California regulations require laboratories to report new cases of COVID-19 to the county public health department. All COVID-19 test results (positive, negative or inconclusive) must be reported. The reports include details like: your name, social security number, and other identifying information. Information about these new infections is used to track this disease statewide and nationwide. Other than this required reporting, your results will be treated confidentially by the study staff. Personally identifying information will not be reported to other departments or agencies. COVID-19 testing is being performed strictly as a clinically required safety measure and not as part of research testing.

What are the costs of taking part in this study?

You will not be charged for any of this research study activities.

Will I be paid for taking part in this study?

In return for your participation in the study, you will be paid as follows:

- If you complete the Pulmonary Function Testing during Baseline Visit (Visit 1), you will be paid $50.
    - If you complete the Pulmonary Function Testing during a separate additional visit, you will be paid extra $50 (total of $100).
- For completing each visit's exercise testing, you will be paid $100 (maximum of $300).
- If you complete the sputum induction procedure, you will be paid $50.
- If you complete each of the albuterol/placebo inhalation and activity monitor sessions, you will receive $50 (maximum of $100).
- If you complete the CT scan procedure, you will be paid $50.
- In addition, if you participate in the longitudinal part of the study, you will be paid $50.
- In addition, you will be paid $40 for every extra visit you have to make to test for COVID-19. The cost of the COVID-19 test will be covered by our research funds.

Overall, if you participate in all parts of the study, you will be paid a total of $770. You will only be paid for the parts of the study that you complete. UCSF must notify the Internal Revenue Service (IRS) when it pays a subject $600 or more in a year, so if you complete all visits and receive $600 within one calendar year, your payment will be reported to the IRS. Your address and Social Security number would be needed for IRS reporting purposes. You will also be reimbursed for parking at UCSF Medical Center for the duration of your participation in this study.

You must return the accelerometer to us before we can pay you for your participation in the study. Also, you must supply your name, address, and social security number so that the accounting office can issue you a check. It usually takes 4 to 6 weeks to receive a check, which will be mailed to your address.

Additionally, if you are traveling from outside of the San Francisco Bay Area (With ID addresses outside of the following counties: Alameda, Contra Costa, Marin, Napa, San Mateo, Santa Clara, Solano, Sonoma, and San Francisco) to participate in this research and require an overnight stay and/or transportation, you will be compensated up to $200 per visit for any travel-related transportation (such as taxi, Uber, shuttle, or airfare expenses) and accommodations (such as overnight hotel or AirBnB) upon providing receipts.

In addition, if you are asked to participate in the optional COVID-19 Visit, you will be paid up to $50 for the visit as detailed below:

- If you complete the COVID-19 questionnaire, you will be paid $20.
- If you complete the blood draw, you will be paid $30.

You will be paid only for the portions of the study that you complete. Your transportation or accommodation costs for participating in the optional COVID-19 visit will not be reimbursed if you are coming from out of area.

What happens if I am injured because I took part in this study?

It is important that you tell your study investigator, Mehrdad Arjomandi, MD if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him [redacted]

Treatment and Compensation for Injury:

If you are injured as a result of being in this study, treatment will be available. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California or the study sponsor *FAMRI,* depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the Office of the Committee on Human Research at (415) 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study investigator about any questions, concerns, or complaints you have about this study. Contact your study investigator:
Mehrdad Arjomandi, MD, [redacted].

If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the Office of the Committee on Human Research at 415-476-1814.

Permission for the optional parts of the research study:
I would like to participate in the following OPTIONAL parts of the study.

If asked, I would like to participate in the COVID-19 Follow-Up Visit of the study. You may contact me in the future for this purpose.

Yes No (Please put your initials in the box indicating your response.)

☐ ☐

CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____ _____
Date Participant's Signature for Consent

_____ _____
Date Person Obtaining Consent