

Cover Page

Official Title: Asthma and childhood obesity: Understanding potential mechanisms and identifying strategies to improve respiratory symptoms

NCT03586544

Date of Document: December 11, 2020



**UNLV Biomedical IRB - Full Committee Review
Modification Approved**

DATE: December 11, 2020

TO: Dharini Bhammar, PhD, MBBS

FROM: UNLV Biomedical IRB

PROTOCOL TITLE: [1131374-20] Asthma and childhood obesity: Understanding potential mechanisms and identifying strategies to improve respiratory symptoms

SUBMISSION TYPE: Revision

ACTION: APPROVED

APPROVAL DATE: December 11, 2020

EXPIRATION DATE: October 19, 2021

REVIEW TYPE: Full Committee Review

Thank you for submission of Revision materials for this protocol. The UNLV Biomedical IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a protocol design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

Modifications reviewed for this action include:

1. Transfer of protocol to UNLV IRB so that UNLV IRB is the IRB of record. Based on the transfer the Parent Permission Form, Assent, and Recruitment Materials were updated under UNLV.
2. Updated the screening form to include the exclusion criteria as separate questions.
3. Updated the Research Team Members by removing a research team member who graduated, Nicholas Ross
4. Updated the Protocol Proposal Form to increase the number of subjects from 50 to 100 subject
5. Updated the questionnaires by removing any questions collecting identifiable information
6. Updated the compensation sections of Protocol Proposal Form, Parent Permission Form, Assent, and Recruitment Materials to change from the Target Gift Card to Visa Forte.

This IRB action will not reset your expiration date for this protocol. The current expiration date for this protocol is October 19, 2021.

PLEASE NOTE:

Attached with this approval notice is the **official Informed Consent/Accent (IC/A) Form** for this study. Only copies of this official IC/A form may be used when obtaining consent. Please keep the original for your records.

If your project has been revised and now involves paying research participants or the procedures for paying participants has been changed, it is recommended to contact ORI Program Coordinator at (702) 895-2794 to ensure compliance with subject payment policy.

Should there be *any* change to the protocol, it will be necessary to submit a **Modification Form** through ORI - Human Subjects. No changes may be made to the existing protocol until modifications have been approved.

ALL UNANTICIPATED PROBLEMS involving risk to subjects or others and SERIOUS and UNEXPECTED adverse events must be reported promptly to this office. Please use the appropriate reporting forms for this procedure. All FDA and sponsor reporting requirements should also be followed.

All NONCOMPLIANCE issues or COMPLAINTS regarding this protocol must be reported promptly to this office.

This protocol has been determined to be a MORE THAN MINIMAL RISK protocol. Based on the risks, this protocol requires continuing review by this committee on an annual basis. Submission of the **Continuing Review Request Form** must be received with sufficient time for review and continued approval before the expiration date of October 19, 2021.

If you have questions, please contact the Office of Research Integrity - Human Subjects at IRB@unlv.edu or call 702-895-2794. Please include your protocol title and IRBNet ID in all correspondence.

Office of Research Integrity - Human Subjects
4505 Maryland Parkway . Box 451047 . Las Vegas, Nevada 89154-1047
(702) 895-2794 . FAX: (702) 895-0805 . IRB@unlv.edu



Department of Kinesiology and Nutrition Sciences

TITLE OF STUDY: Asthma and childhood obesity: Understanding potential mechanisms and identifying strategies to improve respiratory symptoms

INVESTIGATOR: Dharini Bhammar

CONTACT PHONE NUMBER: 702-895-1453 (Office) or 214-770-9382 (Cell)

Purpose of the Study

Your child is invited to participate in a research study. The purpose of this study is investigate how children with mild asthma breathe when they exercise and whether warm-up exercise can reduce breathlessness or exercise-induced asthma when compared with albuterol in children with mild asthma who do and do not have obesity.

Locations of the Study

The first visit is conducted at the Exercise Physiology Lab in MPE 326 at the UNLV Main Campus 4505 S Maryland Pkwy, Las Vegas, NV 89154.

Visits 2-5 will be complete at: 3006 S Maryland Pkwy, Las Vegas, NV 89109.

Visit 2 is conducted at the Children's Heart Center Nevada (3006 S Maryland Pkwy, Suite 690, Las Vegas, NV 89109).

Visits 3 – 5 are conducted at Childrens Lung Specialists pediatric pulmonology clinic (3006 S Maryland Pkwy, Suite 315, Las Vegas, NV 89109).

The dual-energy x-ray scan will take place at the Breast Center at Sunrise (3006 S Maryland Pkwy, Suite 250, Las Vegas, NV 89109).

Participants

Your child is being asked to participate in the study because they fit these criteria:

- 8 – 12 years old
- are in early puberty (Tanner stage < 4)
- are either without obesity (BMI 16th to 84th percentile) or with obesity (BMI >= 95th percentile)
- have physician diagnosed asthma
- have no history of taking oral steroids in the past three weeks or twice in the past year
- have no history of significant mental illness, no history, evidence, or symptoms of cardiovascular disease, metabolic disease, thyroid disease, renal disease, uncontrolled sleep disorders; no musculoskeletal abnormality that would make it difficult to cycle; and no serious health condition that may increase risks of exercise testing

Procedures

If you allow your child to volunteer for this study, your child will be asked to do the following: sign the assent form and complete study procedures over five separate visits. The visits must be done on separate days, with at least 72 hours separating visits 2 – 5.

Participant Initials _____

The procedures are being done solely for the purpose of this study. The tests performed in this study are designed for research, not for medical purposes. They may not be useful for finding problems or diseases. Even though the researchers are not looking at results to find or treat a medical problem, you will be told if they notice something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the tests done in this study are not for medical purposes, we will not issue official reports of the results nor will we share the results directly with your doctor. However, we will provide you with a summary of the key findings and unofficial report copies that you can show to your doctor. We would be pleased to provide whatever further details that you or your doctor might wish.

Visit 1 [2.5 – 3 hours]

This visit will be completed on the UNLV Main Campus in MPE326.

We will collect information related to medications that your child is taking and information about your child's health and asthma during a telephone or email screen with the use of a screening form that will help us decide if you will qualify for the study.

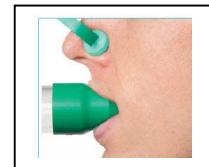
Instructions before the visit: Your child should not consume a heavy meal 2 hours before the visit and not consume any caffeine or engage in heavy exercise for 24 hours before the visit. Your child will need to hold asthma medications for 24 hours. However, if your child needs their medicine you may give it to them and let us know so we can reschedule if needed.

Questionnaires: You will assist your child in filling out the following forms: medical history, physical activity levels, sleep, health in the last 24-hours, diet, puberty, and asthma control.

Measurements: Your child will have height, weight, and measurements of waist, hip, neck and chest circumferences taken. Height and weight will be used to calculate your child's body mass index percentile, which needs to be in a certain range to qualify for this study. We will measure heart rate and blood pressure using an automated blood pressure machine.

Lung function tests: Your child will breathe through a mouthpiece and wear a nose clip during the tests. Your child will be asked to perform several breathing exercises to measure their lung function. This includes four different tests and your child will complete different breathing exercises for each test. The tests are:

1. impulse oscillometry (tells us about airway function)
2. spirometry (tells us how much air your child can breathe out quickly)
3. lung volumes (tells us about the size of your child's lungs)
4. diffusing capacity (tells us about how well oxygen can move from the air into the lungs).



For most of these tests, your child will be sitting in a plastic, body box. For some, they will be seated on a chair outside the body box. The tests are repeated a few times until we have reliable results for each measure.

Response to albuterol: Your child will complete three of the four lung function tests after taking 4 puffs of Albuterol (360mcg). We will measure heart rate and blood pressure before giving albuterol and before your child leaves the lab. If your child has previously had an adverse reaction to albuterol, please let us know and we will reduce the dose from 4 puffs to 2 puffs. If needed, we will consult our physician over the phone for any reactions that occur due to albuterol.

The order of visits 2 – 5 will vary depending on availability of appointments. You will be told what visit to expect once we schedule the visits.

Parent Initials _____

Visit 2 [1.5 – 2 hours]

Visit 2 will be completed at Children's Heart Center Nevada (Suite 690 in the same building as the Childrens Lung Specialists clinic; 3006 S Maryland Pkwy, Suite 690, Las Vegas, NV 89109)

Instructions before the visit: Your child should not consume a heavy meal 2 hours before the visit and not consume any caffeine or engage in heavy exercise for 24 hours before the visit. Your child will take their usual asthma medications prior to this visit.

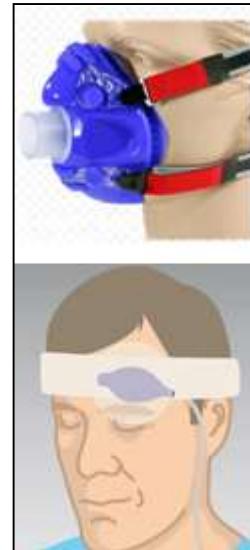
Questionnaires and measurements: Your child will complete a 24hour health history questionnaire.

Pre lung function test: We will assess your child's asthma control on the day of the test using spirometry.

Albuterol administration: Your child will take 2 puffs of albuterol [90 mcg per actuation] after pre lung function tests

Baseline lung function test: We will repeat spirometry 10 minutes after albuterol administration prior to the start of the maximal exercise test to see how your child's lungs responded to albuterol administration. If forced expiratory volume in 1 second is below 75% of predicted during baseline spirometry, the visit will be rescheduled for safety.

Maximal exercise test: Your child will start this test 15 minutes after albuterol administration. The test is completed to assess your child's fitness. During the test, your child will breathe through a mask. There will be stickers (electrodes) on their chest to assess their heart rhythm (EKG) and a cuff around their arm to measure blood pressure. They will also have a sticker on their forehead so we can measure oxygen saturation and heart rate. The goal of the test is for your child to exercise as long as possible. Your child will start pedaling at an easy rate. With every minute, it will become a little harder to move the pedals. We will ask them to rate their breathlessness and exertion during exercise. We will also ask them to take big breaths in during exercise to measure where they are breathing. Your child will only be asked to work to the best of their abilities. They may stop exercise when they wish, because they are feeling tired or uncomfortable.



Post-exercise lung function test: We will repeat the spirometry immediately after the test.

Verification test: Your child will start this test 15 minutes after the conclusion of the maximal exercise test. The goal of this test is for your child to exercise as long as possible at a workload that is a little higher than the highest workload achieved during their maximal exercise test described above. We do this test to verify their maximal exercise capacity. Most children cycle for 2 - 3 minutes at this high workload; however, there is no set time limit for the test. Your child will only be asked to work to the best of their abilities. They will be wearing a mask, the forehead sticker, and the EKG electrodes during this test. They may stop exercise when they wish, because they are feeling tired or uncomfortable.

Visits 3 – 5 [1 – 1.5 hours]

Visits 3-5 will be performed at Childrens Lung Specialists clinic (3006 S Maryland Pkwy, Suite 315, Las Vegas, NV 89109)

Instructions before the visit: Your child should not consume a heavy meal 2 hours before the visit and not consume any caffeine or engage in heavy exercise for 24 hours before the visit. Your child will need to hold asthma medications for 24 hours. However, if your child needs their medicine you may give it to them and let us know so we can reschedule if needed.

Parent Initials _____

Questionnaires: Your child will complete a 24hour health history questionnaire

Pre lung function tests: We will assess your child's asthma control on the day of the test using a test called fraction of expired nitric oxide (FeNO). Nitric oxide is a gas that is released from inflammatory cells in the lung. In this test, your child will breathe out into a machine at a steady pace for 10 seconds. We will then assess lung function using spirometry and impulse oscillometry. If forced expiratory volume in 1 second is below 75% of predicted, the visit will be rescheduled for safety.

The exercise test on each of these three visits will be conducted 15 minutes after either one of the following conditions. Your child will complete all three conditions in this study.

1. Interval warm-up exercise: Your child will be asked to pedal on a bike for 30 seconds while the exercise is difficult and for 45 seconds while it is easy. Your child will do this eight times. There will be a sticker on their forehead to measure their heart rate and oxygen levels. They will be asked to wear a nose clip and breathe through a mouthpiece a few times during the test for breathing measurements. We will ask them to take a big breath in when they are on the mouthpiece. We will also ask how difficult the exercise feels for your child and if they have difficulty breathing during the exercise. They may stop exercise when they wish, because they are feeling tired or uncomfortable.
2. Albuterol: Your child will be asked to inhale 2 puffs [90 mcg per actuation] of albuterol.
3. Control: On this visit, your child will be asked to rest quietly for 15 minutes

Baseline lung function test: 10 min after each condition, we will repeat spirometry and impulse oscillometry.

Exercise test: Your child will be asked to pedal on the bike for 6 – 8 min each. The exercise will feel difficult. During exercise, your child will be wearing a nose clip. They will also have a sticker on their forehead so we can measure oxygen saturation and heart rate. We will ask them to rate their breathlessness and exertion at rest and during exercise. We will also ask them to take a big breath in before and during exercise to measure where they are breathing. Your child may stop exercise when they wish, because they are feeling tired or uncomfortable.

After exercise: We will assess spirometry and impulse oscillometry using breathing exercises for 30 minutes (@ minutes 2, 5, 10, 15, 20, 25, and 30). If there is a change in breathing or if they feel breathless, we will call a physician to evaluate your child. If recommended, your child will be asked to inhale 2 puffs [180 mcg] of a drug (Albuterol). Spirometry will be repeated after 10 minutes to confirm that the asthma has reduced.

Questionnaires Your child will also fill out forms that describe breathlessness and emotions related to breathlessness.

Dual-Energy X-Ray absorptiometry (DXA)

The DXA scan will be performed at the Women's Breast and Diagnostic Center at Sunrise Hospital and Medical Center (Suite 250 in the same building as Childrens Lung Specialists, 3006 S Maryland Pkwy, Suite 250, Las Vegas, NV 89109)

Your child's body composition (fat and lean muscle mass) will be determined by using an FDA-approved bone density measurement machine. Your child will be asked to lie face up, on a padded bed for 7-10 minutes while the scanner arm of the machine passes over their entire body. The scanner will not enclose or touch them, and they can wear their regular clothing (no shoes or metal allowed). The scan will be performed at the Breast Center at Sunrise Hospital and will be scheduled on one of the visits from visits 2-5, when an appointment is available.

Parent Initials _____

Repeating visits

We may ask you to repeat some tests if there are equipment failures or difficulty in collecting data (e.g. child is feeling sick or tired or hungry on a particular day and is unable to give good effort on spirometry), which may take up to three extra visits. As with all testing, you will have the option of whether or not you wish to complete these extra visits. These visits may take an extra 2 – 6 weeks to complete based on scheduling availability and the number of repeat visits.

Benefits of Participation

There *may* be direct benefits to your child as a participant in this study. Your child will receive information regarding your child's lung function and responses to exercise with and without treatment with Albuterol inhaler. Information obtained in this study may help your child's doctors better understand their condition. There will also be no charge for any tests required for the study. Your child's participation will help us learn more about the effects of body weight on pulmonary function and exercise capacity. However, the researchers cannot guarantee that your child will benefit from participation in this research.

Risks of Participation

There are risks involved in all research studies. This study may include greater than minimal risks as listed below:

Holding medicine: We ask your child not to take some of asthma medicines before visits but if you feel like they need their medicine, please have them take it and let us know so we can decide if we need to reschedule.

Spirometry: During spirometry your child may feel a little lightheaded.

Impulse oscillometry, lung volume, diffusing capacity, and FeNO tests: There are no known risks of performing these tests.

Albuterol: Albuterol (Ventolin®) has been known for many years as a well-tolerated drug that expands the airway. It is called a bronchodilator and its list of known side effects is well described. The most common side effects of albuterol (Ventolin®) are sore throat, cough, palpitations (awareness of rapid or pounding heartbeat), chest pain, rapid heart rate, shakiness and nervousness, as well as nausea, increased blood pressure, dizziness and heartburn. These side effects usually go away on their own. Allergic reactions may also occur. Serious allergic reactions may be life threatening.

Maximal Exercise: During maximal exercise, your child will experience discomforts similar to those associated with any type of heavy exercise. There is the possibility of certain changes occurring during the test. They include abnormal blood pressure, fainting, disorder of heartbeat, and in rare instances, heart attack. The risk of serious complication during maximal exercise testing is estimated to be less than 1 per 40,000 such tests in adults. Every effort will be made to minimize these through the preliminary interview and screening, and by observations during testing. A physician or his/her designee will be immediately available during the exercise test. There is a very small possibility of severe breathing problems during or after this test. If this occurs, your child will be immediately treated with a medication (Albuterol) that will reduce their breathlessness. Your child will also be asked to take their regular medications before this test to reduce the risk of breathing problems.

Exercise tests: There is a very small possibility of severe breathing problems during this test. If this occurs, we will call the physician for evaluation and your child will be treated with medication (Albuterol) to reduce their breathlessness. Your child may also experience cough, shortness of breath, chest tightness, wheezing, chest soreness, or headache, however, most people have no symptoms. These

Parent Initials _____

TITLE OF STUDY: Asthma and childhood obesity: Understanding potential mechanisms and identifying strategies to improve respiratory symptoms

symptoms typically disappear after administration of medication (Albuterol). We will monitor their breathing and other vital signs during the test to limit the risks.

In addition, your child may experience discomforts similar to those associated with any type of difficult exercise. Examples of these discomforts may include, but not limited to, shortness of breath, leg fatigue and soreness, and discomfort from sitting on a bike seat. These discomforts have been reported in 2-20% of subjects tested.

Questionnaires: Some of the questions we will ask may make your child feel uncomfortable. They may refuse to answer any of the questions, take a break, or stop participation in this study at any time.

Risks of Radiation: This research study includes exposure to radiation from diagnostic tests in addition to that which your child would receive from standard care. The additional radiation dose your child will get (0.4 μ Gy) is about 1% of the average radiation dose from all sources (natural background radiation, consumer appliances, radon gas, medical tests, etc.) that a person in the United States receives each year. Radiation exposure to a woman's reproductive organs may harm an embryo or fetus.

Loss of Confidentiality: Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential. However, this cannot be guaranteed.

Other Risks: There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers. You will be told if any new information becomes available during the study that could cause you to change your mind about continuing to participate or that is important to your child's health or safety. You may be asked to sign a new permission form that includes the new information if your child decides to stay in the study.

Parent Responsibilities

While your child is a part of this study, the researchers will monitor them during testing for safety. However, it is your responsibility to do the following:

- Ask questions about anything you do not understand
- Follow all pre visit instructions
- Tell the researchers if they take any new medication, even if it is was something purchased over the counter.
- Let the researchers know if your contact information changes or if you cannot keep an appointment.
- Report to the researchers any injuries or illnesses while your child is in the study, even if you do not think it is related.
- It may be uncomfortable for you to see your child have an asthma attack if one does occur.

Responsibility for Costs

Neither you, nor your insurance provider, will be charged for any of the testing done in connection with this research study. However, the standard medical care for your condition (care you would have received whether or not you were in this study) is your responsibility (or the responsibility of your insurance provider or governmental program). You will be charged, in the standard manner, for any procedures performed for your standard medical care. Compensation for an injury resulting from your participation in this research is not available from the University of Nevada, Las Vegas, Children's Heart Center, Childrens Lung Specialists or Sunrise Hospital. However, you keep your legal rights during your participation in this research.

Parent Initials _____

Compensation

The study will take approximately 7.5 - 9.5 hours over 5 days. You will be given a parking permit to park on the UNLV campus. Your child will be compensated \$50 at the end of the first visit (\$20 for consent and questionnaires, \$10 for the lung function test before albuterol and \$20 for the lung function test after albuterol), \$50 on the second visit (\$30 for completing the maximal exercise test, and \$20 for completing the verification test), and \$50 each for the visits 3 – 5 (\$10 for completing the lung function measurement before exercise, \$20 for completing exercise, and \$20 for completing the post-exercise lung function measurement). The total compensation is \$250 if your child completes all five visits. There is no separate compensation for the DXA scan unless you must come in for this on a separate visit because we couldn't get an appointment; in that case your child will be compensated \$20 for this separate visit. If you need to repeat any visits, your child will be compensated at the same rate.

Contact Information

If you or your child have any questions or concerns about the study, you may contact Dharini Bhammar at **702-895-1453 (office)** or **214-770-9382 (mobile)** or **Dharini.Bhammar@unlv.edu**. For questions regarding the rights of research subjects, any complaints or comments regarding the manner in which the study is being conducted you may contact the **UNLV Office of Research Integrity – Human Subjects** at **702-895-2794**, toll free at **888-581-2794**, or via email at **IRB@unlv.edu**.

Voluntary Participation

Your child's participation in this study is voluntary. You or your child may refuse to participate in this study or in any part of this study. Your child may withdraw at any time without prejudice to your relations with the university. You or your child is encouraged to ask questions about this study at the beginning or any time during the research study.

If you decide to stop taking part in this research study, it will not affect your relationship with the Sunrise Hospital, Childrens Lung Specialists, Children's Heart Center, Breast Center at Sunrise, or University of Nevada, Las Vegas staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care.

The researchers may decide to remove your child from this study even if they are interested after completing the screening process if:

- They do not meet our screening criteria.
- They develop a new medical condition, or their medical condition worsens.
- The complications of testing are intolerable.
- The investigator decides that participation in the research is no longer safe for your child.
- They are unable to follow the researcher's instructions.
- You are unable to keep appointments or respond to calls or emails.
- Funding for the project ends or becomes unavailable.

Confidentiality

All information gathered in this study will be kept as confidential as possible. No reference will be made in written or oral materials that could link your child to this study. All records will be stored in a locked facility at UNLV for 3 years after completion of the study. After the storage time the information gathered will be deidentified to remove any information that links your participation and deidentified records may be stored indefinitely.

Parent Initials _____

TITLE OF STUDY: Asthma and childhood obesity: Understanding potential mechanisms and identifying strategies to improve respiratory symptoms

Research Information derived from this study **will not** go into the medical record at Childrens Lung Specialists even if the child is a patient of Dr. Nakamura. You will be given copies of the reports and it is up to you to share these records with your doctor.

Please know that UNLV Exercise Physiology laboratory, Childrens Lung Specialists, Children's Heart Center, and Breast Center at Sunrise Hospital are low traffic areas. However, there may be other clinicians/students/faculty/staff who pass through these areas during testing and/or who may be observing data collection. Please let us know if you have any concern about this.

A description of this clinical trial is available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time

Parent Permission:

I have read the above information and agree to allow my child to participate in this study. I am at least 18 years of age. A copy of this form has been given to me.

Signature of Parent

Child's Name (Please print)

Parent Name (Please Print)

Date

Parent Initials _____