



Parent/Guardian Information Sheet/Consent Form

Perth Children's Hospital

Title	Developing metabolomics profiles to differentiate between healthy, preschool wheeze, and asthma
Short Title	Metabolomic asthma profile
Protocol Number	RGS0000000591
Project Sponsor	
Coordinating Principal Investigator/ Principal Investigator	Dr André Schultz / Dr Stacey Reinke
Associate Investigator(s)	Dr Graham Hall, Dr Ingrid Laing, Prof Robert Trengove, Prof David Broadhurst
Location	Perth Children's Hospital

Part 1 What does participation involve?

1 Introduction

This is an invitation for your child to take part in this research project, *Developing Metabolomics Profiles to Differentiate Between Healthy, Preschool Wheeze, and Asthma*, because your child has asthma or wheeze, or is eligible to participate as a healthy control. Metabolomics is a type of research that measures the substances found in bodily fluids. It is similar to standard urine and blood tests but uses specialised techniques that can measure hundreds of substances at once. This research project is aiming to work out if one can better diagnose and understand asthma by measuring substances in the urine of children with wheeze.

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and research involved. Knowing what is involved will help you decide if you want your child to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether your child can take part, you might want to talk about it with a relative, friend or local doctor.

Participation in this research is voluntary. If you do not wish for your child to take part, they do not have to. They will receive the best possible care whether they take part or not.

If you decide you want your child to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to your child taking part in the research project
- Consent to your child having the tests and research that are described
- Consent to the use of your child's personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

Childhood asthma often begins as wheeze (a whistling sound produced by the airways during breathing) during pre-school age. By the age of 6, about 70% of children will outgrow their wheeze symptoms. Currently it is not possible to predict which preschool children with wheeze will outgrow their symptoms or who will benefit the most from treatment with standard asthma medications.

The aims of the research are to work out if urine can be used to:

- Work out which preschool children with wheeze have asthma and who does not
- Help us to better understand how wheeze and asthma work

Urine will be collected directly into sampling containers or sampling bags. We will then use specialised techniques to measure the metabolites (substances present in extremely small quantities) in the urine. We hope that specific patterns of metabolites in the urine will be able to determine which children have asthma.

Your child may also undergo a physical examination, as well as lung function and allergy testing.

This research is being conducted by researchers from Princess Margaret Hospital, Perth Children's Hospital, the Telethon Kids Institute, Murdoch University and Edith Cowan University.

3 What does participation in this research involve?

Prior to enrolling your child in the study, we will obtain your signature at the end of this form.

Your child may be asked to participate if they are eligible to do so.

This study will involve the following procedures:

1. We will ask you some questions or collect information from your child's medical records such as age, gender, previous and current medications, and history and details of wheeze or asthma. Alongside this, we will write down the time that your child last had something to eat/drink and when they last passed urine.

2. We will ask you to assist your child in providing a urine sample. We will write down the time of sample collection.

3. A paediatric respiratory physician will examine your child for respiratory problems (including wheeze), allergic disorders such as eczema, and other respiratory diseases like cystic fibrosis. The doctor or a researcher will also measure your child's height and weight. They will also check listen to the heart and lungs of your child.

4. A lung function assessment will be performed. When we measure lung function in older children, we ask them to take in big breaths and to blow out hard into our machines (spirometry). Young children cannot do this and so we use lung function tests that only require your child to breath quietly on our machines (FOT). This test uses a sound wave to measure your child's lung function. This works in a similar way to the way fishermen use sonar to find fish. We measure the sound waves that bounce back from your child's lungs. The way they are changed by the lungs gives us information about lung function.

After the first measurement we will administer an inhaled asthma reliever (Ventolin®) to your child and then do another lung function measurement.

5. A skin prick allergy test will be performed. Skin prick testing tells us if your child is allergic to common allergens (such as dust mites, cat, dog, egg, milk, grasses). This is done by skin reactivity tests on your child's arm or thigh (in smaller children). A drop of allergen is placed onto the skin of the forearm. A small prick is made in the skin through the drop. This allows a small amount of allergen to enter the skin. If your child is allergic, a wheal (similar to a mosquito bite lump) will

appear at the site of testing over 10-15 minutes. In some cases this wheal can be large and will cause itchiness that disappears over a period of 1-2 hours. In very rare cases a severe allergic reaction (called anaphylaxis) may occur. Anaphylaxis can occur in the lungs, skin or heart. Symptoms can include swelling of the tongue and/or throat or difficulty talking or a hoarse voice. Anaphylaxis will usually occur within 20 minutes of the test. Anaphylaxis is easily reversed with an "EpiPen". An EpiPen is an auto-injector containing adrenaline. We will use the EpiPen® auto injector, which is an intra-muscular injection of adrenaline for the emergency treatment of anaphylaxis. If this occurs your child would then need to remain in hospital for a minimum of 4 hours observation.

If the test indicates that your child has one or more allergies, we will tell you. Please inform the researcher if your child has ever had a severe allergic reaction or anaphylactic reaction. If it is for one of the allergens that we are testing for, we will not perform the test for that specific allergen. We will only perform the test with the other allergens.

If we are unable to conduct the skin prick test at the first baseline visit, there may be a need to attend another visit at PCH for this to occur.

6. Follow-up sampling. One month after your child's first assessment, we will schedule a home visit, at a time that is convenient for you. During the home visit, a researcher will ask you and your child about their current symptoms and medication and ask you to help your child collect another urine sample. The reason we ask for another urine sample is that the chemicals in urine can change from day to day. By testing another sample, we will be better able to rule out normal changes.

7. If your child has wheeze or asthma, we will also ask that you stay in contact with our study coordinator. If your child has an exacerbation (flare-up) before the study ends, we will ask that you let us know. At that time, if you and your child are willing, we will ask you to schedule a visit at the hospital with us. At that time, the doctor will do another physical examination, check for symptoms, and ask about medications. A researcher will test lung function again and ask that you help your child to provide another urine sample. We will not need to repeat the allergy tests. This study visit will help us to better understand changes that happen during exacerbations.

You will be with your child throughout the entire study appointment.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

Costs and reimbursement: There are no costs associated with participating in this research project, nor will you or the participant be paid. You may be reimbursed for any reasonable travel, parking, meals and other expenses associated with the research project visit, up to \$30 per visit.

4 What does my child have to do?

The study will not interfere with any medical decisions made by your doctors. Your child can continue to take their regular medication.

The researchers may ask your child to fast for a short period of time or drink water only (no more than 3 hours) before providing a urine sample.

This study will involve a home visit arranged one month after the initial assessment. The study coordinator will schedule this with you at the time of the initial assessment. The home visit will be scheduled at a time that is convenient for you and your child.

If your child has wheeze or asthma and experiences an exacerbation before the study ends, we ask that you contact the study coordinator for 1 additional study visit.

5 Other relevant information about the research project

This research project will be carried out at Perth Children's Hospital and aims to recruit 260 participants. There are four study groups in this project:

- 1) 2 – 4 years of age with at least 2 episodes of wheeze and 1 doctor visit for wheeze in the last 12 months.
- 2) 6 – 10 years of age with a diagnosis of asthma.
- 3) 2 – 4 years of age, with no history of wheeze or asthma.
- 4) 6 – 10 years of age, with no history of wheeze or asthma.

Researchers from the Telethon Kids Institute will help in performing some of the tests. Researchers and Murdoch University and Edith Cowan University will analyse the urine samples and data resulting from this study.

6 Does my child have to take part in this research project?

Participation in any research project is voluntary. If you do not wish for your child to take part, they do not have to. If you decide that they can take part and later change your mind, you are free to withdraw them from the project at any stage.

If you do decide that your child can take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether your child can or cannot take part, or take part and then be withdrawn, will not affect their routine treatment, relationship with those treating them or relationship with Princess Margaret Hospital/Perth Children's Hospital.

7 What are the alternatives to participation?

Your child does not have to take part in this research project to receive treatment at this hospital.

8 What are the possible benefits of taking part?

There will be no clear benefit to your child from participating in this research. However, if the research is successful, it may help to better diagnose childhood asthma at an earlier age in the future.

9 What are the possible risks and disadvantages of taking part?

Urine Collection: The collection of urine is not known to have any serious risks. If your child shows any distress with providing a urine sample, then simply stop and let the investigators know.

Lung Function Measurements: As well as lung function changes the Ventolin may cause increases in your child's heart rate and in some children may result in mild tremors. These effects are generally mild and only last an hour or so. The lung function tests are not generally difficult to do, however some children may take longer to learn the test. Some children may not wish to perform the lung function test.. If your child shows distress during this procedure, the investigators will stop.

Allergy Testing: If your child is allergic, a wheal (similar to a mosquito bite lump) will appear at the site of testing over 10-15 minutes. In some cases this wheal can be large and will cause itchiness that disappears over a period of 1-2 hours. In very rare cases a severe allergic reaction (called anaphylaxis) may occur. Anaphylaxis can occur in the lungs, skin or heart. Symptoms can include swelling of the tongue and/or throat or difficulty talking or a hoarse voice. Anaphylaxis will usually

occur within 20 minutes of the test. Anaphylaxis is easily reversed with an “EpiPen”. An EpiPen is an auto-injector containing adrenaline. We will use the EpiPen® auto injector, which is an intramuscular injection of adrenaline for the emergency treatment of anaphylaxis. If this occurs your child would then need to remain in hospital for a minimum of 4 hours observation.

10 What will happen to my child’s test samples?

The urine samples collected will be stored at the Telethon Kids Institute and then sent to Murdoch University or Edith Cowan University for testing. Although Murdoch and Edith Cowan Universities will be the primary centres for metabolomics analyses, samples may also be analysed by researchers at partner laboratories at the University of Western Australia (UWA), and the future Australian National Phenome Centre. We may also send some samples to Imperial College in London.

12 Can my child have other treatments during this research project?

We will ask you about any treatment that your child is on during the study. It is important to tell the study doctor and the study staff about any treatments or medications the participant may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. Please let us know if new treatments are added or if any treatments are stopped prior to the sample being collected.

13 What if my child is withdrawn from this research project?

You can withdraw your child from this research project at any time, please notify a member of the research team before withdrawal.

If you do withdraw consent during the research project, the study doctor and relevant study staff will not collect additional personal information from your child, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the researchers up to the time your child withdraws will form part of the research project results. If you do not want them to do this, you must tell them before your child joins the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include finding robust answers to our research questions before the end of the study.

15 What happens when the research project ends?

Please let the investigators know if you would like a summary of the research findings at the end of the study. The study is expected to run for approximately 2 years. We will store any leftover urine samples for up to 10 years. We may want to use such leftover sample for future research. Please let the investigators know if you would rather the leftover sample to be destroyed.

Part 2 How is the research project being conducted?

16 What will happen to information about my child?

By signing the consent form, you consent to the study doctor and relevant research staff collecting and using personal information about your child for the research project. Any information obtained in connection with this research project that can identify your child will remain confidential. For purposes of data storage your child's name will be replaced by unique identifying codes. The key to the code will be stored on a secure hard-drive on a password protected computer in a secure research facility. Only two researchers involved in the study will have access to the key. Your child's information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

Information about your child may be obtained from their health records held at this and other health services, for the purpose of this research. By signing the consent form you agree to the research team accessing health records if they are relevant to participation in this research project.

Data from this study will be stored using the REDCap secure, web-based database system. Access to the RedCAP survey questions and entered data is provided only to the research investigators and is password protected. Computers will require individual username and password access to use.

Your child's health records and any information obtained during the research project are subject to inspection for the purpose of verifying the procedures and the data. This review may be done by the relevant authorities, the National Health and Medical Research Council, the institution relevant to this Participant Information Sheet, the Child and Adolescent Health Service, or as required by law. By signing the Consent Form, you authorise release of, or access to, this confidential information to the relevant research personnel and regulatory authorities as noted above.

It is anticipated that the results of this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that your child cannot be identified, except with your permission.

Any information obtained for the purpose of this research project that can identify your child will be treated as confidential and securely stored. It will be disclosed only with your permission, or as required by law.

17 Complaints and compensation

If your child suffers any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment. If your child is eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

18 Who is organising and funding the research?

This research is being conducted by researchers from Princess Margaret Hospital, Perth Children's Hospital, the Telethon Kids Institute, Murdoch University, and Edith Cowan University.

The research is funded by a Telethon – Perth Children's Hospital Research Fund grant from the Western Australia Department of Health.

19 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of the Child and Adolescent Health Service.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

20 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if your child has any medical problems, which may be related to involvement in the project (for example, any side effects), you can contact the principal study doctor, please see below. You are also able to contact Sherlynn, research assistant on 0402047078 for any study appointment related queries.

Clinical contact person

Name	André Schultz
Position	<i>Paediatric Respiratory Physician</i>
Telephone	6456 2222
Email	<i>Andre.schultz@health.wa.gov.au</i>

For matters relating to research at the site at which your child is taking part, the details of the local site complaints person are the same as the clinical contact person.

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

The Director of Clinical Services at Perth Children's Hospital on (08) 6456 2222.

Consent Form – Parent/Guardian

Title Developing metabolomics profiles to differentiate between healthy, preschool wheeze, and asthma
Short Title Metabolomic asthma profile
Protocol Number RGS0000000591
Project Sponsor
**Coordinating Principal Investigator/
Principal Investigator** *Dr André Schultz / Dr Stacey Reinke*
Associate Investigator(s) *Dr Graham Hall, Dr Ingrid Laing, Prof Robert
Trenrove, Prof David Broadhurst*
Location Perth Children's Hospital

Declaration by Parent/Guardian

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to my child participating in this research project as described and understand that I am free to withdraw them at any time during the project without affecting their future health care.

I understand that I will be given a signed copy of this document to keep.

I would like my child's sample to be kept in long-term storage for future studies.

Name of Child (please print) _____

Name of Parent/Guardian (please print) _____

Signature of Parent/Guardian _____

Date _____

Name of Witness* to

Parent/Guardian's Signature (please print) _____

Signature _____

Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher[†]

I have given a verbal explanation of the research project, its procedures and risks and I believe that the parent/guardian of the participant has understood that explanation.

Name of Study Doctor/
Senior Researcher[†] (please print) _____

Signature _____

Date _____

[†] A senior member of the research team must provide the explanation of, and information concerning, the research project.

Note: All parties signing the consent section must date their own signature.