



Participant Information Sheet for Parents / Guardians (OxSOCRATES Online)

Thank you for your interest in this study. We would like to invite your child to take part. This sheet provides some information about the study. Please take the time to read it carefully and discuss it with your child to see if they are interested in taking part. You may also wish to discuss it with friends, family or your GP. We have included an age-specific information sheet for your child to read too.

Our contact details are given at the end of this document. Please contact us if anything is unclear or you would like more information and to let us know if your child is interested in taking part.

What is the purpose of this study?

Adults with risk factors like high blood pressure or cholesterol are more likely to develop heart disease but we know very little about what causes the risk factors themselves. They don't affect everybody but when they do occur, the age at which they first appear and their severity varies greatly. Although clear risk factors don't usually emerge before middle age, our hearts and blood vessels begin to change in childhood in ways that may eventually lead to illness. We need to find ways to stop this process early so that young people do not become adults with a high risk of illnesses such as heart disease or stroke.

For most of us, the changes to our organs build up over decades before illness occurs. By that time, it may no longer be possible to reverse the damage to our organs. Doctors can treat such disease but a much better solution would be to prevent the damage in the first place. Detailed studies in children and adolescents are needed to make this possible. The British Heart Foundation has funded us to carry out such a study. We will look at how different levels of physical activity and of body fat storage affect the health of children. We will also examine how becoming more active improves their health. Although we all know exercise has health benefits, it is not clear what changes in our bodies are responsible for this, particularly in childhood. By addressing how lack of exercise and increased body fat make us less healthy and how the body becomes healthier through increased exercise, our study should help us to develop effective early prevention of heart disease and its associated conditions. This is more important than ever today, as obesity and low activity levels are becoming more common in children and adults.

Why has my child been asked to take part?

They have been invited to take part because they are healthy and aged between 11 and 18 years. We will check that they fit our criteria based on their height, weight, and physical activity levels.

Does my child have to take part?

No, it is voluntary. They will need you to sign the consent form to take part, so please decide together. You do not have to give a reason for your decision and, if you agree to take part, you may change your minds at any time. If your child has dairy allergies, type 1 diabetes or there are any reasons why they cannot safely exercise or have an MRI scan, then they will not be able to take part, unfortunately. If you think they could be pregnant then you do not have to tell anyone, but please do not agree to take part. Your decision will never affect the standard of care that your child will receive from us or any other caregivers.

What does the study involve?

We will initially contact you and your child via phone/video call to discuss the study, to address any questions and check that it is safe to proceed. We will then ask for permission to record your child's height, weight, month and year of birth, and complete questionnaires on your child's activity levels. We will provide you with instructions to collect these measurements accurately at home, so that we can check whether your child is eligible for the next stage of our study. There may also be a possibility that these measurements can be taken at your child's school.

Once these measures have been completed we will inform you whether your child fits our criteria or not (suitable age, physical activity levels, height, and weight). If they meet our criteria, we will invite both of you to our university laboratory for the next stage of the study where we will ask you to sign a consent form. If your child is under 16 years old, they will be asked to sign an assent form too. If they are 16 years old or older, then both of you will be asked to sign a consent form. During this visit we will measure your child's height and weight again and waist and hip circumferences along with other measures including a fitness assessment, wearing a 36-hour blood pressure monitor, and a physical activity watch for a week.

Once these measurements have been collected, your child will then be allocated to one of these pathways, depending on their physical activity height, and weight.

Pathway 1 involves the visit to our university laboratory (as detailed above), a single visit (~5 hours) to the John Radcliffe Hospital for an MRI scan, an echocardiogram and some blood tests then a follow-up at 1-year, which includes another 36-hour blood pressure recording and wearing an activity watch for a week. Children on this pathway will be asked to complete an online risk factor questionnaire, which will be repeated at the 1-year follow-up. They will also be asked to do an online diet assessment (a questionnaire on three separate days) at the start and end of the year.

Pathway 2 is the same as pathway 1 except children will also be asked to take part in a 2-month fitness programme (3x 1-hour sessions per week), where they will be supervised by our fitness experts over a video link online. Most exercise sessions will be done at home in this way but there may be an option for them to do some online sessions during normal PE lessons, depending on which school they go to. During this period, they will wear the activity watch for another week and have a further diet assessment. At the end of the fitness programme, they will be asked to attend a second MRI and echocardiogram session (~5 hours) with the same measures, undertake a further fitness test, have a further 36-hour blood pressure recording, wear the activity watch again and repeat the risk questionnaire and diet assessment. These steps are detailed below.

36 Hours Ambulatory Blood Pressure

Your child will be asked to wear the blood pressure monitor. This is similar to blood pressure devices you may be familiar with that inflate a cuff on your arm but it is designed to take a number of measurements over 36-hours, giving a more accurate assessment. It cannot be worn in water, so we will show your child how to remove and refit it for bathing. This device will be set up by one of the research team and collected by you from the university facilities, usually after the exercise test. Once 36 hours have elapsed, you will return it to the research team at the university facilities. We will give you directions beforehand for picking up and dropping off the device.

Physical Activity Watch

Your child will be provided with a lightweight physical activity watch, which is worn on their wrist for a week. The battery in the device is powerful enough that it does not need to be charged and is completely waterproof. This allows your child to continuously wear the watch throughout the day and night. It measures how much movement your child achieves and what type of intensities these movements are performed at.

Questionnaires

Your child will be provided with an access code for our online questionnaires, allowing them to answer questions for us over a secure online connection using a web browser. Some questionnaire sections relate to the wider family and we hope that you will be able to help your child answer these. The questions cover a wide range of factors that influence our risk of developing health problems, such as diet, physical activity, exercise, and stress. Although we hope that it will be possible to complete the questionnaire in the comfort of your home, there will be opportunities to go through the answers with the team later.

School Information

Upon your child's first visit to university facilities, we will ask you what school your child attends. We will then write to your child's school asking them to provide some background information about your child. This will include their name, sex, date of birth, free school meal eligibility, and exam results. Together with the questionnaires, this background information will allow us to check that our results are meaningful for all children. If your child's school requests proof of parental consent to provide this data, then a copy of your signed parental consent will be given to your child's school. If your child's school is unwilling to provide this information it will not affect your child's participation in the study. Furthermore, if your child took part in *Fit to Study* (PI: Heidi Johansen-Berg; University of Oxford) and has the necessary data, we will try to maximise the value of those measures to see, for example, how their fitness has changed over time.

Fitness Testing

You and your child will be invited to come to university testing facilities where we will ask them to undergo a fitness test (VO₂ max test) lasting about 20 minutes. This involves your child cycling on a stationary exercise bike, or running on a treadmill, while wearing a sterile face mask for expired air analysis. This will measure the maximum volume of oxygen that they can use in order to get an objective measure of their fitness. This is a standard test that is used regularly in our laboratory and in NHS healthcare and an experienced researcher will be present throughout the test to ensure your child's safety. Following the test, we will ask them to complete a short questionnaire to assess their enjoyment of sports and exercise. Please bring some comfortable / sports clothing and shoes to the fitness test that are suitable for your child to wear while exercising. During

this time, we will also measure their body composition (fat, muscle *etc.*) to allow comparison to the images we acquire during the MRI procedure (see below). This takes less than a minute and involves standing on a machine similar to weighing scales. If your child has not completed all of the pre-screening PE lesson before volunteering to take part, the fitness test visit will also be a good opportunity for them to do so.

Before the MRI and Echocardiogram Session

Things that people consume can affect our measurements. For example, caffeine, alcohol, tobacco and other recreational drugs can have lasting effects that alter the results. Therefore, we will ask that your child does not consume any of these substances for at least 24 hours prior to their visit. Similarly, physical exercise and food choice on the day preceding the study are important. We will ask that your child does not exercise formally after 3pm on the day prior to their visit until their visit is over and that they eat a standard meal at a precise time the evening before. You will be provided with a list of options for this meal and we should be happy to reimburse its cost. After this, your child should not eat again and should drink only water until after the visit unless their visit is in the afternoon. If so, we would like them to eat a standard breakfast (a piece of bread or toast, with only a small quantity of butter or margarine and no other topping) at least 6 hours before their scan and then consume no more food until after the study.

We will also provide your child with a urine collection kit and instructions so that they can collect a sample of their urine on the morning of their visit to our MRI department. Ideally, we will arrange for them to do this when they arrive, but it could be done at home before you come to the department. This sample will give us information on how they process the foods in their diet. Studies have shown that the breakdown products from food in urine differ significantly between people and some patterns of those products have been linked to their risk of developing diseases like heart disease. Your child's urine sample will be processed to remove the cells before it is stored as detailed below and then analysed for levels of breakdown products from food. In addition, we will be very grateful if they could provide us with a small stool sample. Again, this will usually be on the same day or sometimes on the day before the visit. This will help us find out whether the bacteria that live in the gut are important for keeping people healthy. The samples will be analysed to quantify the number and type of bacteria living in your child's gut. They will be provided with a collection kit for this and detailed instructions on how to do this cleanly and safely. We anticipate that children under the age of 16 years are likely to need their parents' help with this.

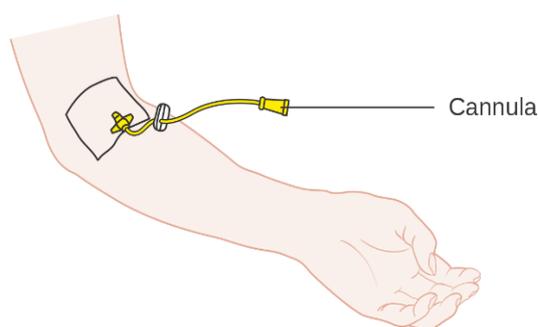
MRI and Echocardiogram Session

You and your child will then be invited to come to the Oxford Centre for Magnetic Resonance Research (OCMR), based at the John Radcliffe Hospital in Oxford. A safety screen will be done and consent will be confirmed at this stage. Then, we will ask your child to have a magnetic resonance imaging (MRI) scan of their heart, blood vessels, muscles, and body fat (initial scan ~1½ hours, which includes three opportunities to stand up and stretch their legs, then two further 15 min scans), an echocardiogram (ultrasound of the heart taking ~15 mins), ingest a cream and sugar drink, and have blood tests (<1 min each time), as detailed below. We will ensure that the total amount of blood taken over the course of the visit does not exceed the recommended research safety limit for your child of 3 mL per kg body weight. For example, if they weigh 40 kg, we will not take more than 120 mL (~6 tablespoons) in total during their visit. They will be able to watch a film or listen to music during the MRI. You should plan for each visit to OCMR to start either in the morning at a standard time e.g. 08:00 am, or in the afternoon at a standard

time e.g. 13:00 pm and take about 5 hours altogether. This is because the MRI scans and blood tests will occur over a four-hour period to detect the response to the meal.

MRI scanners take pictures of the body using a large magnet, radio waves and a computer, without touching the body. The MRI machine is shaped like a short, open-ended tunnel. Your child will be asked to lie down on a flat scanning bed that slides into the tunnel. During the scan, your child will be asked to lie quite still and to wear headphones to protect their hearing and so that we can communicate with them. From time to time, they may be asked to hold their breath briefly.

The MRI and echocardiogram will give us a lot of information about how your child's heart and blood vessels function when they are resting. However, it has become clear that sometimes the differences between healthy people and less healthy people only appear when their bodies are being challenged. High-calorie meals are a good way to test this in a way that reflects the lifestyle of many of us. We will ask your child to consume a dairy-based (cream) high-fat, high-sugar drink similar to a milkshake. The effect on their heart and blood vessels will be determined by MRI and measurements of their blood pressure. Other responses will be measured using blood tests. For example, we will measure their insulin response (the hormone that controls the delivery of food's energy-content to the organs). In order to do this, we will ask your child to have a cannula (a narrow plastic tube) placed temporarily in a surface vein in their hand or arm. This is illustrated below:



The cannula is placed using a small needle that is then removed, leaving the tube behind. It will allow us to take blood samples before the meal and at a number of time points after the meal without needing to puncture the skin again or cause discomfort. It will be removed at the end of the study visit. In this way, we will build up a picture of how a range of chemical messengers and hormones in the body respond to a high fat, high sugar meal.

Genetic Risk

Finally, some of the blood collected during the study will be analysed for variations in a range of genes that may increase the risk of obesity and diseases such as heart disease. Each individual variation contributes a very small additional risk of these disorders and can usually be considered a variation of normal. In other words, none of the genes that we are testing for could be used to make a specific diagnosis of a disease. However, we will study how collections of genes influence our health and fitness.

Fitness Programme

Some of the children may be asked to take part in a 2-month fitness programme, run online by video link with our expert fitness trainers. We will provide all equipment and technologies needed for your child to do this at home, with a parent present. It may be possible for some children to do some sessions at school as part of their PE lessons as well.

One-year Follow-up

After 12 months, all of the children will be asked to have a further blood pressure check, again using the 36-hour device, wear an activity watch for a week, and do further questionnaires online. The devices will be fitted and returned to the university facilities. The results will help us determine whose health changed the most over the year.

What are the benefits of taking part?

There is no immediate benefit to you or your child from taking part in this study. However, we will try to make it an educational experience for your child. We should like to offer your child vouchers (e.g. Amazon) worth £30 in gratitude for their help with our study. The vouchers for those who take part in the fitness programme will be worth more (£40) to recognise their additional effort. We should also be pleased to reimburse the cost of travel for your visits to the hospital and the expense of the standardised evening meals.

What are the disadvantages or risks of taking part?

There is very little risk or disadvantage associated with taking part in this study. However, your child may experience some minor discomfort due to blood sampling. Some people may experience nausea after consuming the high fat, high sugar drink but this should be short-lived. MRI is safe and non-invasive and does not involve ionizing radiation (x-rays). However, because it uses a large magnet, MRI scans are not suitable for everyone. Your child and any parent/guardian accompanying them into the MRI room will be asked standard safety questions to determine if they are able to take part. For example, we will not offer your child an MRI scan if they have a pacemaker, mechanical heart valve, or cochlear implant and would need to investigate further if they have other metal in their bodies before proceeding.

There is no evidence that MRI is harmful to unborn babies but, as a precaution, the Department of Health advises against scanning pregnant women, unless there is a clinical benefit. Therefore, we will ask about the possibility of pregnancy in all post-pubertal girls who take part and any women who wish to accompany them into the MRI room. If they think there is a possibility that they might be pregnant, they will not be able to take part. We do not test for pregnancy routinely.

If you think your child might be claustrophobic, please discuss this in advance with the researcher, or let the radiographer or operator know before your scan. As some of the scans are noisy, headphones and earplugs will be provided for anyone entering the MRI room to make this quieter. It is important that these are fitted correctly as they are designed to protect hearing. For their comfort and safety, anyone entering the MRI room will also be provided with appropriately-sized pocket-less, metal-free "pyjama-style" tops and trousers. Most underwear and socks may be worn underneath but we would ask that underwired bras are removed. Ideally, non-metallic bras should be worn on the day. Please avoid any fabrics that contain metallic threads or have been silver impregnated (often marketed as anti-microbial/bacterial or anti-odour). Metal jewellery, including body piercings, must also be removed. Eye shadow and mascara must also be avoided, since some types contain materials that can interact with the magnetic field. Makeup removal wipes will be provided to remove makeup worn to the hospital. Lockers are provided to secure personal belongings and clothing. Participants will be introduced carefully to the scanner and allowed to leave at any stage. Whilst in the scanner, participants will have easy access to a call button should they wish to stop the scan or speak with the radiographer or operator.

It is important to note that we do not carry out scans for diagnostic purposes, only for research. Our scans are not routinely looked at by a doctor and are therefore not a substitute for a doctor's appointment. Occasionally, however, a possible abnormality may be detected. In this case, we would have the scan checked by a doctor. If the doctor feels that the abnormality could be medically important, we will contact you directly to recommend that they have a hospital (NHS) diagnostic scan arranged. You would not be informed unless the doctor considers the finding has clear implications for your child's current or future health. All information about your child will be kept strictly confidential.

If your child is less than 16 years-of-age, we will contact you or your nominated responsible adult before each online exercise session to check that they can go ahead with the session and that an adult will be present in the home during the session.

What will happen to the data provided?

The "research data" will be data provided by you and your child during the course of the study. Our use of personal data (allowing direct identification, which are name, date of birth, and contact details) and sensitive data (which are health details, ethnic group, DNA sequencing) will be minimised. Most data will be kept in a form where only a secure code can be used to identify the data as belonging to your child. A file stored securely away from all other data will link this code to your personal, identifiable details for the duration of the study. The link code will be destroyed 6 months after publication. All electronic data, including MRI imaging, will be kept on firewall and password-protected computers and any paper information e.g. consent forms will be stored in lockable cabinets in swipe-card secured buildings. Data will only be accessed by the research team. Responsible members of the University of Oxford may be given access for monitoring / audit of the study to ensure we are complying with guidelines. In line with regulations, the research data and consent forms will be securely archived for at least 10 years after publication.

What will happen to any samples that are given?

Blood, urine and stool samples will be collected and stored securely in departmental freezers. After DNA/RNA extraction for the genetic analysis, the cells in the samples will be disposed of. Analyses will be carried out at the University of Oxford. It is common for new scientific tests to emerge after studies have been carried out. We recognise that the samples given by your child are a precious resource and would like the opportunity to make the best of this. In order to do so, we will ask that their samples be gifted to us so that we can carry out further analyses of any sample-derived material in the future. For example, we might test for a newly discovered hormone that affects appetite or new genes might be added to the risk score.

Although our study includes some clinical blood tests, they will not be routinely assessed by doctors because for scientific reasons, the analyses of blood tests from many participants will be done in batches much later than they were collected. The results will be significantly out-of-date by the time they are available and will not, therefore, be clinically useful to you.

What will happen to the results of the study?

The results of the study will be available after it finishes and will usually be published in a medical journal or presented at a scientific conference. The data will be anonymous and participants will not be identified. We should be pleased to make the results and publications available to you.

Who is organising and funding the research?

This study has been funded by the British Heart Foundation and carried out by Dr. Alexander Jones (PI), Department of Paediatrics, the University of Oxford.

Who has reviewed the study?

All research studies are checked by an ethics committee to ensure the research is conducted safely and to the best standards. This research has been reviewed by, and received favourable opinion from, a subcommittee of the University of Oxford Central University Research Ethics Committee.

Data Protection

The University of Oxford is the data controller with respect to your child's personal data, and as such will determine how those data are used in the study. The University will process your child's personal data for the purpose of the research outlined above. Research is a task that we perform in the public interest.

Further information about your rights with respect to your personal data is available from <http://www.admin.ox.ac.uk/councilsec/compliance/gdpr/individualrights/>.

What if there is a problem?

If you have a concern about any aspect of this study, please contact the Principal Investigator (Dr. Alexander Jones) on 07423 474923 or by emailing OxSOCRATES@medsci.ox.ac.uk. He will do his best to answer your query and should respond within 10 working days, giving you an indication of how he intends to deal with it. If you remain unhappy or wish to make a formal complaint, please write to the Chair of the Medical Sciences Inter-Divisional Research Ethics Committee at Research Services, University of Oxford, Wellington Square, Oxford. OX1 2JD, or by emailing ethics@medsci.ox.ac.uk. They will seek to resolve the matter in an expeditious manner.

Further information and contact details

You and your child should feel free to ask any questions that you wish, at any time during your participation in this study. We should be pleased to answer them or address your concerns, provide you with up-to-date information about procedures in the study, or provide you with the background research this study is based on. The Principal Investigator can be contacted as follows:

Name: Dr. Alexander Jones
Telephone: 07423 474923
Email: OxSOCRATES@medsci.ox.ac.uk

If your child would like to take part, please contact us. You will be asked to provide verbal consent for us to gain information on your child's eligibility for the study and then read and sign a consent form. Copies of this information sheet and the consent form will be given to you to keep and filed in the study records.

Thank you for taking the time to read this information sheet.