



Participant Information Sheet for 16 to 18 Year-Olds (OxSOCRATES Online)

Thank you for your interest in this study. We would like to invite you to take part. This sheet provides some information about the study. Please take the time to read it carefully to see if you are interested in taking part. You must discuss this study with your parent(s)/guardian(s) and they must also consent to your participation before you can volunteer to take part. You may also wish to discuss it with friends, family or your GP.

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 you are 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 have I been asked to take part?

You have been invited to take part because you have responded to our online advert.

Do I have to take part?

No, it is voluntary. You do not have to give a reason for your decision and, if you agree to take part, you may change your mind at any time. If you have dairy allergies, type 1 diabetes or there are any reasons why you cannot safely exercise or have an MRI scan, then you will not be able to take part, unfortunately. If you think you 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 you receive from us or any other caregivers.

What does the study involve?

We will initially contact you and your parents/guardians to organise a phone/video call to discuss the study, to address any questions and check that it is safe to proceed. If you live independently, we will also need your parents/guardians contact details and their consent for your participation. We will then ask for permission to record your height, weight, month and year of birth, and questionnaires on how active you are. We will provide you with instructions to collect these measurements accurately at home, so that we can check whether you are eligible for the next stage of our study. There may also be a possibility that these measurements can be taken at your school.

Once these measures have been completed we will inform you whether you fit our criteria or not (suitable age, physical activity level, height, and weight). If you meet our criteria, we will invite both you and your parents/guardians to our university laboratory for the next stage of the study where we will ask you and your parents/guardians to sign a consent form. During this visit we will measure your 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, you will then be allocated to one of these pathways, depending on your physical activity levels, 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 the activity watch again. Participants 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 you will also be asked to take part in a 2-month fitness programme (3x 1-hour sessions per week), where you 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 you to do some online sessions during normal PE lessons, depending on which school you go to. During this period, you will wear the activity watch again and have a further diet assessment. At the end of the fitness programme, you 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

You 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 you 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 university facilities, usually after your 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

You will be provided with a lightweight physical activity watch, which is worn on your 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 you to continuously wear the watch throughout the day and night. It measures how much movement you achieve and what type of intensities these movements are performed at.

Questionnaires

You will be provided with an access code for our online questionnaires, allowing you 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 your parent(s)/guardian(s) will be able to help you with 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 first visit to university facilities, we will ask you to let us know what school you attend. We will then write to your school asking them to provide some background information about you. This will include your 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 school requests proof of signed consent to provide this data, then a copy of your signed parental consent form will be given to your school. If your school is unwilling to provide this information it will not affect your participation in the study. Furthermore, If you previously took part in *Fit to Study* (PI: Heidi Johansen-Berg; University of Oxford) and have the necessary data, we will try to maximise the value of those measures to see, for example, how your fitness has changed over time.

Fitness Testing

You will be invited to come to university testing facilities where we will ask you to undergo a fitness test (VO₂ max test) lasting about 20 minutes. This involves you cycling on a stationary exercise bike, or running on a treadmill while wearing a disinfected and sterile face mask for expired air analysis. This will measure the maximum volume of oxygen that you can use in order to get an objective measure of your 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 safety. Following the test, we will ask you 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 you to wear while exercising. During this time, we will also measure your 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 you have 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 you to complete it.

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 you do not consume any of these substances for at least 24 hours prior to your visit. Similarly, physical exercise and food choice on the day preceding the study are important. We will ask that you do not exercise formally after 3 pm on the day prior to your visit until your visit is over and that you 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, you should not eat again and should drink only water until after your visit unless your visit is in the afternoon. If so, we would like you to eat a standard breakfast (a piece of bread or toast, with only a small quantity of butter or margarine and no other toppings) at least 6 hours before your scan and then consume no more food until after the study.

We will also provide you with a urine collection kit and instructions so that you can collect a sample of your urine on the morning of your visit to our MRI department. Ideally, we will arrange for you to do this when you arrive, but it could be done at home before you come to the department. This sample will give us information on how you process the foods in your 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 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 you could provide us with a small stool (poo) sample. Again, this will usually be on the same day or sometimes on the day before your visit. This will help us find out whether the bacteria that live in your gut are important for keeping people healthy. The samples will be analysed to quantify the number and type of bacteria living in your gut. You will be provided with a collection kit for this and detailed instructions on how to do this cleanly and safely.

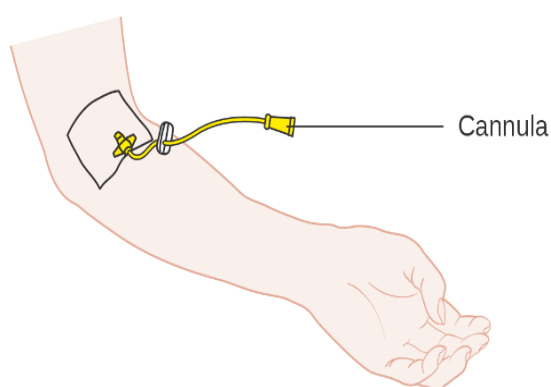
MRI and Echocardiogram Session

You and your parents/guardians 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. There, we will ask you to have a magnetic resonance imaging (MRI) scan of your heart, blood vessels, muscles, and body fat (initial scan ~1½ hours which includes three chances to stretch your 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 of 3 mL per kg body weight. For example, if you weigh 40 kg, we will not take more than 120 mL (~6 tablespoons) in total during the visit. You 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. You will be asked to lie down on a flat scanning bed that slides into the tunnel. During the scan, you will be asked to lie quite still and to wear headphones to

protect your hearing and so that we can communicate with you. From time to time, you may be asked to hold your breath briefly.

The MRI and echocardiogram will give us a lot of information about how your 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 you to consume a dairy-based (cream) high fat, high sugar drink similar to a milkshake. The effect on your heart and blood vessels will be determined by MRI and measurements of your blood pressure. Other responses will be measured using blood tests. For example, we will measure your insulin response (the hormone that controls delivery of food's energy-content to the organs). In order to do this, we will ask you to have a cannula (a narrow plastic tube) placed temporarily in a surface vein in your hand or arm. This is illustrated below:



This 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 you 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 you to do this at home. Depending on which school you go to, it may be possible to take part in some sessions at school as part of your PE lessons. If you take part in the fitness programme, you will be asked to come back at the end of the programme to repeat the fitness assessment, MRI, blood tests and range of measures that you had prior to the programme. This will allow us to see if the fitness programme has improved your health.

One-year Follow-up

After 12 months, you 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 from taking part in this study. However, we will try to make it an educational experience. We should like to offer you vouchers (e.g. Amazon) worth £30 in gratitude for your 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, you 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. You will be asked standard safety questions to determine if you are able to take part. For example, we will not offer you an MRI scan if you have a pacemaker, mechanical heart valve, or cochlear implant and would need to investigate further if you have other metal in your body 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 you 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 you have a hospital (NHS) diagnostic scan arranged. You would not be informed unless the doctor considers the finding has clear implications for your current or future health. All information about you will be kept strictly confidential.

What will happen to the data provided?

The “research data” will be data provided by you 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, and DNA sequences) 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 you. 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 I give?

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 your samples are a precious resource and would like the opportunity to make the best of this. In order to do so, we will ask that your 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 personal data, and as such will determine how those data are used in the study. The University will process your 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) 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 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 you would like to take part, please contact us. Your parents/guardians will be asked to provide verbal consent for us to gain information on your 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 and your parents/guardians to keep and filed in the study records.

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