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RESPECCT

RESpiratory syncytial virus and S. pnEumoniae Challenge Coinfection sTudy

PARTICIPANT INFORMATION SHEET

Thank you for your interest in our study. This leaflet explains the study and a member of the team will also discuss it in full if you are interested in participating. Please ask us if you have any questions. You may want to talk to other people about the study – please do so. Take your time to decide if you want to be involved.

What is this study?

This study is looking at two different germs: a bacterium called *Streptococcus pneumoniae* ('pneumococcus', Spn) and a virus called *Respiratory syncytial virus* (RSV). These germs can cause a variety of symptoms from cold-like illnesses to chest infections or sepsis. It is thought that having one of these germs means that it is easier to catch the other and this study is trying to see if and why that might be true. Participants in this study will be exposed first to one and then the other of these germs and undergo tests to look at the response of their immune system. Participants are paid for their involvement.

Who are we?

We are researchers at The University of Oxford and The Liverpool School of Tropical Medicine (LSTM). We have been studying lung infections using healthy volunteers for over ten years to provide world-leading research into the pneumococcus germ using methods called an Experimental Human Pneumococcal Challenge (EHPC) model. More than 2000 participants have already been safely studied using our methods.

What is the purpose of this study?

Both pneumococcus and RSV are common germs worldwide causing infections with symptoms that range from mild colds and ear infections to serious pneumonia and sepsis. When someone is exposed to both, which is very common in winter, it might affect how likely they are to develop infection or how serious their symptoms are. It is important to understand this relationship better so that future studies on treatments or vaccines can be performed.

The strains of germ used are:

- RSV: Respiratory Syncytial Virus-A Memphis 37 at a dose of 5,000 plaque forming units per nostril
- Pneumococcus*: Streptococcus pneumoniae* serotype 6B at a dose of 80,000 colony forming units per nostril

RSV and pneumococcus have been safely used individually in separate outpatient challenge studies (where participants stay in their own homes but attend the study site for regular visits). However, this will be the first time both germs are used in the same challenge study. For this reason, the first 10 participants in this study will be asked to stay at a research facility for up to 10 days for inpatient observation.

Do I have to take part?

No. Taking part in this study is entirely voluntary. If you decide to participate, you can withdraw from the study at any time. This will not affect your healthcare.

Who can take part in the study?

We are looking for up to 113 healthy volunteers. We will check for reasons that may put you at higher risk for taking part in the study. We also make sure that your participation will provide helpful information to us. If we find any reason that you may be at higher risk of infection, then we will not invite you to take part.

You are potentially eligible if:

- You are aged between 18-55 (inclusive)
- You are able to consent for yourself
- You speak English fluently
- You are not pregnant and are willing to practice adequate birth control measures during the study (females of childbearing potential)
- You are willing and able to self-isolate for 10 days for a part of the study period

You are not eligible if any of the following apply to you:

- You are already enrolled for another clinical trial involving medications or vaccinations
- You suffer from chronic respiratory disease (such as asthma requiring an inhaler, COPD, bronchiectasis or sleep apnoea)
- You have previously received an RSV or pneumococcal vaccine
- You have had a live vaccine within the last 28 days
- You have medical conditions that increase your risk of serious infection, such as cancer, diabetes, asthma on regular medication, major heart/lung disease, rheumatoid arthritis or suffer from suffer from recurrent ear infections
- You are a current smoker (including vaping or recreational drugs), have recently given up smoking (within the past 6 months) or were a heavy smoker in the past
- You have been admitted to hospital with pneumococcal infection within the last 10 years
- You are on any medication that might impact the study results, such as chemotherapy, steroids, Roaccutane, GTN or blood-thinners, or have taken antibiotics within the last 28 days
- You are allergic to penicillin or amoxicillin
- You are pregnant, breast-feeding or intend on becoming pregnant during the study
- You have a direct caring role to people at high-risk of infection: those under 5 or over 65 years old, those classified as extremely clinically vulnerable, or you are a healthcare worker
- You plan to travel overseas within 21 days after the first study intervention

What happens if I choose to take part?

If you choose to take part in the study, we will ask you to meet the research team in-person. At this visit, we will check if you are suitable, and you will be given the opportunity to ask questions. If you are happy to proceed, we will ask for your written signed consent. Following this, you will have a clinical examination and tests which may include looking for evidence of previous RSV infection. The study involves further 8 in-person visits (9 visits including the initial visit above). These are spaced out over approximately 10 weeks with most of the visits happening in the first three weeks.

During the study, everyone will be exposed to both the pneumococcus germ and the RSV germ through drops in the nose, seven days apart. Each participant will be randomly allocated to which germ they receive first.

If you are in the first up to 10 participants enrolled into the study you will need to self-isolate in the Oxford Experimental Medicine Clinical Research Facility (Churchill Dr, Headington, Oxford OX3 7LE) with a clinical team on-site for up to 10 days following the RSV exposure. This is to make sure that there are no safety concerns with being infected with two different germs. You will be reimbursed for this time.

All other participants will have to self-isolate at home for up to 10 days, after being exposed to RSV (regardless of whether you are exposed first or second). You must not leave your home during this period, except to visit the research team or in an emergency. You should sleep in your own room and maintain social distancing from others in your household. Rooms must be well-ventilated, and doors closed. You should use any shared kitchen or bathrooms without other members of your household present and clean it thoroughly after using them. This is important to minimise the risk of accidentally transmitting RSV to another person.

You should wear a fluid resistant surgical facemask (provided) when outside. When travelling to the clinic during this period you should ideally walk wearing the provided facemasks, cycle, drive yourself or take a private taxi, also wearing this mask. Free parking will not be available at hospital sites, please use paid parking facilities or arrange to be dropped off. You will be reimbursed for travel expenses.

Those who will be resident on site for 10 days, we advise arriving in a taxi or being dropped off, parking will not be available for that length of time.

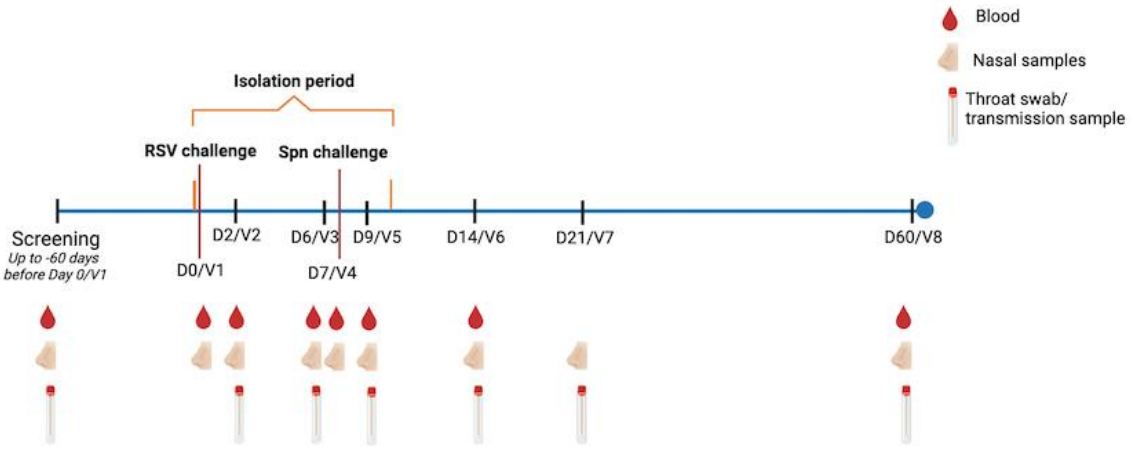
You will not need to self-isolate after the Spn challenge.

How can I look after my mood during isolation?

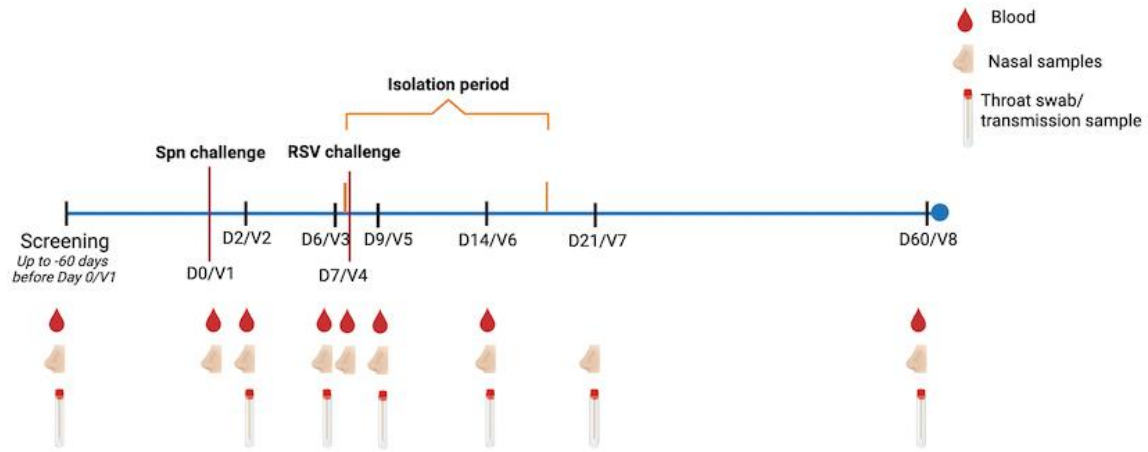
It's only natural that you may feel anxious about taking part in this study. You may be concerned about some of the study procedures or about having to self-isolate in an unfamiliar environment away from your usual support networks, or away from your usual routine. It is important you consider the effect of the study on your mood prior to taking part. We will work with you to think about ways in which we can support you whilst participating in this study. Additionally, we would recommend you arrange regular contact with your family and friends by telephone or video call as a means of added support. We will be asking you to complete a mood questionnaire prior to confirming your eligibility for the study and maybe also performed at other time points within the study period.

Timeline of study visits and procedures

1. ***If you are randomised to be challenged with RSV first***



2. If you are randomised to be challenged with Spn first



What happens at each visit?

Visit 0: Screening visit

A member of the research team will discuss the study with you individually or in a group session. You will have the opportunity to ask questions and discuss the study directly with a researcher in private following the presentation. This initial discussion may either take place at Visit 0 (when consent is obtained) or may take place prior to Visit 0. Procedures may occur over 2 separate visits.

If you are happy to take part in the study, you will be asked to complete a questionnaire to demonstrate understanding of what the study involves before signing a consent form. We will ask you questions to assess whether you are eligible to take part in the study. The overall screening visit takes around 2 hours.

We will ask routine questions about your medical health, your vaccination history and medications you are taking. We will take your blood pressure, heart rate and temperature, and we will carry out a brief examination. This is all done to make sure you are fit and well. Females of childbearing potential

will have a urine pregnancy test. We will take blood tests, throat swabs, nasal wash, nasal cells, a urine sample (where relevant) and a COVID-19 test.

If we need further information about your medical history to confirm your eligibility, we may access your electronic patient record or request your GP to complete a questionnaire or provide your medical summary before screening visit. You will be randomly allocated which germ to be given first and informed of the allocation.

Visit 1 and Visit 4: Challenge visits

We will check you are happy to continue and that you are feeling well prior to challenge. Another blood test will be taken. You will be asked to sit slightly reclined for 15 minutes and then the germ (either pneumococcus or RSV) will be introduced to both nostrils by dripping in a small liquid sample with a dropper. You will be asked not to swallow so the fluid stays in the nose for as long as possible. The challenge visits take around 2 hours each.

You will go home with a study pack including:

- A course of antibiotics to keep with you in case you are unwell
- A thermometer to check your temperature at home
- A safety information sheet
- A study contact card
- Nose/saliva sampling swabs, instructions and storage bags

If you have received the RSV germ in your nose at the first visit, you need to start your self-isolation. At home you will need to keep a daily symptom diary for 21 days after the first challenge. The study team will review your symptoms every day both remotely and during face-to- face follow up visits You should inform the study team about any moderate/severe symptoms as soon as possible. Details on clinical symptom definitions will be given to you.

Whilst at home, you will take some samples from your own nose and saliva (we will train you on how to do this) and keep them in our secure bags in the freezer. We will ask you to bring these samples to the clinic at your next follow-up appointment.

Seven days after the first challenge, you will return for the second challenge (Visit 4). This will be very similar to Visit 1 but you will receive the other germ which you did not receive the first time.

Inpatient observation participants only

If you are one of the first 10 participants enrolled, you will be invited to the inpatient observation part of the study. You will be requested to stay in a dedicated research facility for up to 10 days after you have had your RSV challenge (regardless of whether you receive this as your first or second challenge). The research teams will check your vital signs, collect blood and nasal samples and make sure you feel ok. You will take some samples from your own nose and saliva. You will be compensated appropriately for your inpatient stay. If all 10 slots are filled, we may ask you to volunteer to be a ‘back-up’ for

inpatient observation. We will inform you of the dates of the observation period in advance to check you will be available for the whole time. You will not need to self-isolate after the Spn challenge.

Follow-up visits

You will return to the clinic for further checks on your vital signs, to review any symptoms you might develop and more nose, throat and blood tests at several timepoints after the first and second challenges as shown in the table above. In total you will have around 9 study visits (including screening and challenge visits).

What samples do we collect from you?

We collect nose, throat, saliva, urine and blood samples to look at the germs and your immune response.

Nasal wash: We gently squirt a little salty water into your nose. After a few seconds the water runs out into a sample bowl. This will tell us about the germs in your nose and your immunity.

Throat swab: We take a small cotton swab and wipe the back of your throat in a circular motion. This is to test for germs in your throat.

Nasopharyngeal swab/Saliva: We use a small cotton swab and wipe the back of your throat and nose to test for COVID-19 and other respiratory germs. Saliva may be used as an alternative.

Nasal cells: We insert a very small and narrow plastic spoon (about the size of a toothpick) into the inner surface of the nose that is withdrawn in a sweeping motion to collect small cells. We will perform this twice on each nostril. This is to look at your immune response.

Blood samples: We take blood samples from a vein in your arm (using a needle). We will take up to 80mL (about the same as 5 tablespoons) during a visit. This amount of blood is safe to have taken in one go, and your body will replace this blood quickly. This is to look at your immune response.

Urine: In females of childbearing potential, a urine pregnancy test will be performed at screening, Visit 1 and Visit 4.

Self-sampling during the period after challenge:

We will ask you to take the following samples in the week following both your first and second challenge visit. We will ask you to take a sample 2, 6 and 12 hours after challenge, and then daily until 7 days after the challenge visit. We ask that you take the test at approximately the same time each day.

We will provide you with a step-by-step guide (RESPECCT self-sampling guidance) for the obtention of home samples. We will ask you to obtain **Nasopharyngeal/Nasal swab, Nasosorption and Saliva samples.**

What are the risks from this study?

Challenge with RSV or pneumococcal bacteria: Because the germs we expose you to are live, there is a very small risk of infection to you or your close contacts. However, both germs have been used in previous studies in healthy adults with no serious side effects. You may however get cold-like symptoms, headaches, earaches, a cough or a fever.

We provide a safety pack as described above and you will have 24-hour access to the research team by phone. This includes clear safety precautions and what to do if you feel unwell. Everyone who tests positive for the pneumococcus germ will take a course of antibiotics at the end of the study, or if they feel unwell, before that.

We also offer RSV screening to your household contacts (defined as those who share a kitchen with you at home) to better understand how RSV might spread between people. The **Household Contact Screening Information Letter and Consent Form** provides more information for your household contacts. Results from these swabs will not be used for future research.

Blood sampling: The risks associated with blood sampling are minimal, but this may cause temporary pain, bruising and/or bleeding to your arm. The blood sampling will be performed by trained healthcare professionals. In the rare circumstance that we notice anything unusual or medically significant about your blood then we would let you know and ask your permission to inform your GP.

Nasal sampling: There are limited risks related to these samples. During a nasal wash, you may swallow a small amount of salty water, however, this is harmless. The nasal cell sample is slightly uncomfortable and may make your eyes water briefly. Sometimes a small amount of blood can be seen on the sample probe, however, it is rare for it to cause a nosebleed.

Throat swabs/Nasopharyngeal/nose swabs: These samples may make you feel some discomfort. A small amount of blood can be seen occasionally on the nasal sample probe, however, it is rare for it to cause a nosebleed.

Incidental medical findings

Since we carry out several medical tests throughout the study, it is possible that we detect previously unknown health issues (*e.g.* high blood pressure, abnormal blood results such as infection with hepatitis B or C and human immunodeficiency virus [HIV]). This will be discussed with yourself and with your permission, your GP informed for ongoing follow up.

In the UK, healthcare professionals are legally obliged to report any new suspected cases of hepatitis B and hepatitis C to the UK Health Security Agency (UKHSA). If you are found to have hepatitis B or C, we will be required to send a report to the UKHSA, including your name and personal contact information. It's important to note that you cannot opt out of this due to UK reporting requirements.

What happens to my samples?

The samples taken in this study will be processed in the Liverpool School of Tropical Medicine, Liverpool University Hospitals NHS Foundation Trust, Oxford Vaccine Group, University of Oxford, Oxford University Hospitals NHS Trust and Pfizer.

Samples will be taken to look at your immune response to the virus as well as the bacterium and whether you are carrying either in your nose after exposure. These experiments may involve the extraction of molecules, such as DNA, which make up the genes in your cells. These tests can be used to see if there are genetic factors that affect protection or susceptibility to these bacteria or viruses.

The blood samples we collect to assess your eligibility and safety will be processed in an NHS laboratory and results from these samples are connected to your NHS record. Your details and results from these samples are safeguarded under the NHS Trust's data protection policy and will only be accessed during the study by the researchers to assess your safety and eligibility.

We will also ask for your consent to retain leftover samples to be used for future ethically approved research in the UK and overseas. This consent will be requested separately. If you consent, samples are anonymised and will be transferred to a research tissue bank at the end of the study. You can decide whether or not you agree to genetic material being stored, however, your DNA is unique to you so it can never be completely anonymous. These samples will be transferred to a research tissue bank held at the University of Oxford. The stored samples will be analysed, as and when new technology becomes available, or when new scientific questions arise relating to protection and susceptibility of disease and carriage. If you agree, these samples would be stored indefinitely.

What if there is a problem?

The research team is available to contact 24/7 by phone. Please contact us as soon as possible if you are unwell or if you develop any symptoms including, but not exclusive to, sore throat, earache, headache, fever, cough, breathlessness, lack of taste or smell. We would also like to know about any new health or medication changes. Any medical care you need will be provided by the NHS.

The study is sponsored by the University of Oxford and is insured in the unlikely event that you suffer any harm as a direct consequence of your participation in this study.

What if I change my mind or want to stop?

If you do start the study, you are free to stop at any time and without giving a reason. If you decide not to take part, or to withdraw from the study, this won't affect your future healthcare.

If you decide to stop or lose capacity to consent to being in the study, we will only continue to use the samples that have already been taken and information that we have already collected from you – no further samples or data will be collected. You are free to request that your samples are destroyed at any time during or after the study. You will be paid for the visits completed up to that point.

The study team may stop your involvement in the study for the following safety reasons:

- If you develop a condition that is in the exclusion criteria
- If you start a new medication that is prohibited

- If you become pregnant
- If you are unable to follow study instructions or the team are unable to contact you.

The participant would be withdrawn from the study. Identifiable data or tissue already collected with consent would be retained and used in the study. No further data or tissue would be collected or any other research procedures carried out on or in relation to the participant

What if I wish to report a concern?

If you wish to report a concern about any aspect of the study, you can contact the research investigators info@ovg.ox.ac.uk. You can also alternatively contact the Chief Investigator Prof Maheshi Ramasamy Maheshi.Ramasamy@paediatrics.ox.ac.uk or you may contact the sponsor, the University of Oxford, RGEA office on 01864 616480, or the director of RGEA, rgea.complaints@admin.ox.ac.uk. Reporting a concern will not affect the medical care you receive now or in the future.

Would my taking part in this study be kept confidential?

All information that is collected about you during the research will be coded with a study number and kept strictly confidential. Any information about you that leaves the clinic would have your name and address removed so that you could not be recognised, except for your signed consent form and letters sent to your own GP. To enrol into this study, you are required to consent for us to contact your GP.

We will write to your GP to inform them when you enrol in the study and when you complete it, so they can update your medical records accordingly. Your GP may also be asked to share information about your medical history and give access to any other medical records as required to ensure there are no medical reasons that would prevent you from taking part. We would only notify your GP of the results of any medical tests with your permission.

Responsible members of the University of Oxford, the relevant NHS Trusts involved in the research may also be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations. No one else will be told that you are involved in the study.

What are the benefits of taking part?

You will be a valuable part of a research study that we hope will eventually lead to the development of new methods to prevent or treat respiratory infections.

How much will I get paid?

All participants will be reimbursed for their time, travel and for inconvenience based on the following figures:

Time per visit*	£40 per hour
Travel expenses per visit*	£30
Sample collection per visit*	£20
Diary completion	£60
Inpatient period per day	£200
Self-isolation period per day	£150

*If screening procedures are split, reimbursement will be as per one visit. If you are eligible for enrolment, all visits are completed, the full 10-day isolation period is observed and the required symptom e-diaries are completed, then you may be entitled to reimbursement of between £2580 - £3130.

What will happen to my data?

United Kingdom data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford, based in the United Kingdom is the 'data controller' and is responsible for looking after your information and using it properly. Your personal information will be kept confidential and handled in accordance with data protection laws in the UK. We will be using information from you and your medical records to undertake this study.

We will use minimum amount of personally identifiable information. Data will be collected and held by the Oxford Vaccine Group. It will be accessible to staff at the Oxford Vaccine Group, responsible staff from the University of Oxford, regulatory authorities, independent auditors which may be appointed by Sponsor and funder in collaboration, who may monitor/audit the data collection process. The database servers are held by the sponsor. We will keep identifiable information about you such as contact details for a minimum of 5 years after the study has finished. The need to store this information for longer will be subject to ongoing review. De-identified research data will be stored indefinitely.

Data may be transferred outside of the UK e.g., to Pfizer Inc in the United States, where data protection laws may differ from the UK. Data that are transferred elsewhere will be pseudo anonymised (meaning any identifiable information will be replaced in a way that does not allow you to be directly identified).

We may take a photocopy of your ID (driver's licence, passport or national ID card) for identification purposes and we will ask for payment information at the screening visit. We will securely retain copies until the end of the study. Your bank details will be stored for a minimum of 7 years in line with financial requirements. If you only complete online screening or telephone screening (before informed consent) your data will only be kept to the end of the trial.

During your screening, you would be asked to provide your National Insurance number (or passport number if you do not have a national insurance number). This would be entered on to a national database which helps prevent volunteers from taking part in too many clinical trials. The Over-

volunteering Prevention Service (TOPS) database is to ensure safety of all our participants in this study and therefore if you are unwilling your information submitted on TOPS you would not be able to take part in our study. If you withdraw from the study before you receive a challenge, the database will show you never received a challenge. Only the study staff and other medicines research units can use the database. We may call other units, or they may call us, to check your details. Data entered by us in TOPS is determined based on whether you receive a challenge or not. If you receive a challenge, this data will be retained in TOPS. If we need to contact you about the study after you have finished it, but we can't because you have moved or lost contact with your GP, we might be able to trace you through the information in the database. Further information can be found at:
The Over-Volunteering Prevention System - Health Research Authority (hra.nhs.uk)

At the completion of the study, unless you consent otherwise (e.g., if you request to be informed of other studies), your personal details will not be used to contact you other than in exceptional circumstances concerning your safety. If you consent to take part in another study carried out by the Oxford Vaccine Group personal information and medical information including blood test results may be accessed to avoid unnecessary repetition.

UK data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at

https://compliance.web.ox.ac.uk/individual-rights

You can find out more about how we use your information by contacting info@ovg.ox.ac.uk

What will happen to the results of this study?

The results of this research study may be presented at scientific meetings or conferences and published in a scientific medical journal. This can take approximately 2 years after the study is completed. Your individual results would not be identifiable nor would you be identified in any report or publication. A copy of the main research publication will be shared with you and will also be published on our website.

Who has reviewed this study?

This study has been reviewed by the study sponsor (the University of Oxford). This research has been looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given favourable opinion by East of England – Cambridge South Research Ethics Committee.

Who is organising and funding the study?

This study is sponsored by the University of Oxford and funded by Pfizer Inc.

Further information and contact details

We hope this information sheet has given you enough information to make decision on whether to volunteer for this study. If you are interested in participating, you do not need to make a final decision straight away.

If you have further questions about the study that you would like to discuss with our team, please contact us at:

Email: info@ovg.ox.ac.uk

Tel: 01865 611400

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