



Patient Name
Patient Address

Participant Information sheet: Patients aged 16-17 years
Version 1, 08.03.18

Research study to determine the genetic causes of Primary Sclerosing Cholangitis and childhood Autoimmune Liver Disease

Dear patient,

You are being invited to take part in the **UK PSC Study** (www.uk-psc.com). This is a UK-wide project aimed at finding factors (genetic, as well as markers in the blood) involved in causing Primary Sclerosing Cholangitis (PSC) in adults and autoimmune liver disease in children. The UK PSC Study is part of the National Institute for Health Research (NIHR) research programme that provides NHS research infrastructure to support research into rare diseases.

The Chief Investigator leading the study is Dr Palak Trivedi, Honorary Consultant Hepatologist at the University of Birmingham. Your liver doctor is a member of the broader research team.

Before you decide whether you would like to participate, it is important that you understand the reason for the research and what participation in the study will involve.

Please take time to read the following information carefully, to ensure that you have understood what is involved in the study and have asked any questions that you have.

Feel free to discuss the study with your family or close friends. Please contact us if you have any questions; we would be happy to hear from you. You can find our contact details at the end of this document.

Your decision to enter the study is entirely voluntary and you may choose not to participate. If you decide not to participate, this will not affect your future medical care.

More information, including Frequently Asked Questions, can be found on our website, **www.uk-psc.com**

Why have I been invited? Why is it important?

In children and young people different types of autoimmune liver disease are seen including Primary Sclerosing Cholangitis, Autoimmune Sclerosing Cholangitis and Autoimmune Hepatitis. You have been invited because you are known to have autoimmune liver disease and are currently under the care of a liver doctor.

I have already joined the study. Why are you contacting me again?

We are contacting you to ask you to update your consent to the study, by signing the new consent form, and to provide further blood samples, for DNA extraction and/or to measure markers in the blood associated with childhood autoimmune liver disease. We would also be grateful if you could update your health information.

What is the purpose of the study?

We do not know what causes childhood autoimmune liver disease or PSC in adults. However, there is evidence that genetic factors are important. By studying DNA (genetic material) obtained from affected patients, we hope to achieve a better understanding of how genetic factors contribute to these diseases.

Only half of the genes for rare diseases are currently known. Discovering genes causing rare diseases is the start of a new journey. Accurate tests for rare diseases can be developed to obtain more rapid diagnosis. Once the gene causing a rare disease has been identified, the search for effective treatments can start.

Who is organising and funding this study?

This study is organised by the **UK PSC** national research collaboration (www.uk-psc.com). The investigators include doctors looking after adults with PSC and children with autoimmune liver disease across the UK.

The Chief Investigator is Dr Palak Trivedi. It is jointly sponsored by the University of Cambridge and Cambridge University Hospitals NHS Foundation Trust. It has also been reviewed and approved by the Cambridge South Research Ethics Committee (REC reference 08/H0305/45).

The infrastructure support to maintain recruitment and data analysis is from support to the Investigators by the NIHR Birmingham Biomedical Research Centre, as well as funded research collaborations with Industry.

What happens if I participate in the study?

If you decide to participate in the study, we will ask you to do the following:

- Initial, date and sign the UK PSC Informed Consent Form (version 4).
- Complete the UK PSC Participant Questionnaire (version 3) about your autoimmune liver disease and your health in general.

To donate the following samples:

- **Two blood samples**, which will be taken at your liver clinic appointment. One sample will be used to extract DNA and the other will be used to measure markers in the blood associated with these diseases. The blood samples requested are of approximately 2 teaspoons
- For your liver care team to return to the UK PSC research office:
 - The completed participant questionnaire (using the freepost envelope provided)
 - The signed Informed Consent Form and blood samples (using the sample transport box provided).

- The address to send the samples and documents to is:
The UK PSC Study
Box 238
Department of Medical Genetics
Lv 6 Addenbrooke's Treatment Centre
Cambridge Biomedical Campus
Hills Rd
Cambridge, CB2 0QQ
- You will find the Informed Consent Form and participant questionnaire in the recruitment pack that the research team has given to you.

What will happen next?

When we have received your signed consent form, we will do the following:

- We will obtain information about your health from your medical records;
- We will extract a sample of your DNA from your blood sample (DNA is the material that contains all of your genetic information);
- We will analyse your DNA to obtain information about your genetic make-up;
- We will extract serum from your second blood sample, and use it to analyse markers in the blood associated with childhood autoimmune liver disease;
- We will use information about your health and genetic make-up in large-scale studies to look for genetic factors that contribute to PSC and childhood autoimmune liver disease.

In addition, if you have ever had a liver biopsy, we may request a copy of the report from the pathology department from the hospital where this was done. Additionally, if available, we may request that tissue is transferred to a central laboratory for further analysis. However, you will not be asked to have a liver biopsy for the purpose of this study, and the biopsy will not be re-reported.

What information will be collected about me?

If you participate in the study, we will collect your name and contact details so that, if we need to, we can contact you during the study. We will also collect information about your health and major life events. This information will include your current and past illnesses; admissions to hospital; investigations such as blood tests, scans or radiological investigations, and any treatments you might have received. We will continue to collect this information into the future, so that we can see how autoimmune liver disease affects you over time. This will include annual information from your liver doctors. In the event of your death, we will request information about when and why it happened.

With your permission, we will obtain information about your health and major life events from the following sources:

- Your medical records held by your hospital;
- Your medical records held by your GP surgery;
- Your medical records stored in NHS data centres

NHS data centres are organisations that collect and store information about how people use the NHS, such as information about outpatient clinic appointments; visits to A&E, and admissions to

hospital. NHS data centres also hold information about the date and cause of death, which they obtain from the Office of National Statistics. The NHS data centres include NHS Digital in England, the Information Services Division (ISD) for NHS National Services Scotland, the NHS Wales Informatics Service and the Health and Social Care Board Northern Ireland.

To collect health-related information about you, we will use your NHS number (or CHI number, if you live in Scotland). For example, we will send your NHS (or CHI) number to the NHS data centre using a secure system. The NHS data centre will find information linked to your NHS (or CHI) number and send it to the research team, using the same secure system. The advantage of using the NHS (or CHI) number is that we can collect information without using your name. Any information obtained from your hospital will be collected by NHS staff or members of the UK-PSC research team or at your own hospital.

What will happen to my DNA sample in the future?

We will isolate, analyse and store your DNA and other components from the donated samples for use in studies to help us understand how genetic factors contribute to childhood autoimmune liver disease and PSC in adults. We may measure a range of chemicals in these samples and may determine your genetic code.

Genes are made out of DNA. RNA is the version of the DNA code that the body uses to direct how proteins are made. We may determine the DNA/RNA code of the samples taken. This may include determining the sequence of all or part of your DNA code.

If we use all of your DNA sample during the study, we may ask you to provide another sample of blood for extraction of DNA. It is your decision whether to provide additional samples. If you decide not to provide additional samples, your decision will not affect the healthcare you receive in any way. At the end of the current study, some of your DNA sample may be frozen and stored in an approved biorepository for further analysis in future, ethically-approved studies.

With your permission, some of your DNA sample may be shared with other investigators who are not part of the current study including profit-making (commercial) companies and not-for-profit organisations (such as research charities), universities or hospitals, in the UK or abroad. However, it will only be shared if this has been approved by a 'Sample Access Committee', on behalf of the UK PSC study. Samples shared with other researchers will be anonymised so that you could never be identified. Furthermore, other researchers will be made to sign a legally-binding Sample Access Agreement in which they commit to protect the confidentiality of participants and use the sample for research purposes only.

What will happen to information collected about me?

If you participate in the study, information collected about you will be used to help us understand how genetic factors contribute to childhood autoimmune liver disease. It will be used to improve understanding of rare diseases, in general. This information will be stored in a secure computer database, called the UK PSC database, and your identity will be protected. The database will have the same level of protection as confidential information stored by your own hospital. Access to the UK-PSC Database is tightly restricted.

Only the following individuals are allowed to see all of the information stored in the database:

- Authorised members of the UK-PSC and registered biorepository research teams;
- Regulatory authorities, such as the Research and Development (R&D) Department at Cambridge University Hospitals NHS Foundation Trust or your local hospital.

Identifiable information (such as your name, address and NHS or CHI number) will be destroyed ten years after the study has ended. Non-identifiable information about you (such as the results of medical investigations) will be retained indefinitely for further analysis in future, ethically-approved studies, undertaken by UK-PSC.

With your permission, information about you may be shared with other investigators who are not part of the current study, including profit-making (commercial) companies and not-for-profit organisations (such as research charities), universities or hospitals, in the UK or abroad. However, information about you will only be shared if this has been approved by a 'Data Access Committee' on behalf of the UK PSC Study. Information shared with other researchers will be anonymised so that you could never be identified. Furthermore, other researchers will be made to sign a legally-binding Data Access Agreement in which they commit to protect the confidentiality of participants and use the information for research purposes only.

What will happen to my genetic information?

Genetic information obtained from your DNA sample will be stored indefinitely in the UK-PSC Database, as described above. With your permission, your genetic information will also be stored indefinitely in a secure electronic archive called the European Genome-phenome Archive (EGA), maintained by the European Bioinformatics Institute (EBI) in Hinxton, Cambridge, UK.

Genetic information stored in the EGA will be anonymised, so that you could never be identified. Anonymised genetic information stored in the EGA may be shared with other researchers who are not part of the current study. Other researchers might be from profit-making (commercial) companies and not-for-profit organisations, such as research charities, or universities or hospitals, in the UK or abroad. However, these researchers will be made to sign a legally-binding Data Access Agreement in which they commit to protect the confidentiality of participants and use the information for research purposes only.

Do I have to take part?

Participation in this study is entirely voluntary. If you decide not to participate, this will not affect your future medical care. Even if you agree to participate, you may still withdraw from the study in the future, without having to give a reason.

What are the advantages of taking part?

There are no immediate advantages in terms of the care you currently receive in the clinic and on the ward. However, you will be making a contribution to science and future improvements in NHS care. The results from this study may help us to achieve a better understanding of the genes that cause PSC in adults and autoimmune liver disease in children. This may result in improved treatment and management of these conditions for all patients in the future.

What are the risks and disadvantages of taking part?

The only disadvantage of taking part in the study is having blood taken. There may be some discomfort from having blood taken and there is a small risk of bruising, inflammation or fainting. To minimise risk, we will aim for blood samples to be taken by experienced staff at the same time as the blood tests requested by your doctor in the clinic.

Will my participation in this study be kept confidential?

Yes, the UK PSC Study, conforms to strict data-handling and access procedures and uses secure data systems developed to NHS standards. All aspects of this study comply with the Data Protection Act (1998).

As described above, information collected as part of the study will be stored in a secure computer database, called the UK-PSC Database, which has the same level of protection as confidential information stored by your own hospital. Access to the UK-PSC Database will be restricted to authorised members of the UK-PSC and registered biorepository research teams (if indicated), and regulatory authorities from Cambridge University Hospitals NHS Foundation Trust or your own hospital. Identifiable information (i.e. your name, address and NHS or CHI number) will be used only to access your medical records or contact you in the course of the study. Identifiable information will be destroyed ten years after the end of the study. Non-identifiable information (such as the results of medical investigations) will be stored indefinitely.

If you join the study, you will be assigned a unique study number. Your DNA sample will be labelled with this number, not your identifiable information. Information shared with other researchers or the EGA will also be labelled with this number, not your identifiable information. In this way, samples and information shared with other researchers or the EGA will be anonymised, so that you could never be identified. During the study and for ten years after the study has ended, samples and shared information will be 'linked-anonymized' because the study number will be linked to identifiable information kept secret in the UK-PSC Database. Dr Palak Trivedi (Chief Investigator), of the University of Birmingham, will act as the main custodian of the data.

Will I be told the results of tests performed on my samples?

We will not routinely tell you the results of tests performed on your samples. However, if we inadvertently discover that you have a genetic abnormality which is known to cause a particular disease, we will inform your liver doctor. The liver doctor will meet with you to discuss the finding. You will then be referred to a genetics doctor to confirm the finding and plan further management. This policy is based on the Genomics England project. For a list of the particular genetic abnormalities that would prompt us to contact your liver doctor, please see the Genomics England website (<http://www.genomicsengland.co.uk/>).

Please be aware that the government has extended the genetic test insurance moratorium until 2019. This means there are restrictions that prevent providers from using genetic test results to deny people insurance cover until that set date. **Even so, if you do not want us to inform you and your doctor of any genetic abnormality that we may find, please leave Box 11 on the consent form empty.**

What will happen to the study results?

The results of the study will be published in scientific journals and presented at medical meetings both locally and nationally. You will not be identified in any reports or publications.

Results that have been published in the scientific literature will also be reported on the UK-PSC website (<http://www.uk-psc.com/>). Furthermore, important results will be reported in the newsletters or on the websites of UK-based patient support groups, such as PSC Support and the PSC Trust and these can also be made available to you at your request.

Will I receive any money for taking part?

You will not receive any funding for taking part in this study and no travelling expenses will be reimbursed, as the study visit will be timed to coincide with a routine visit to the hospital.

What happens if a scientific discovery is made using my donated samples?

If you participate in the study, any sample you donate to the study will be given as an absolute and non-returnable gift, meaning it is given without conditions and without receiving payment. For example, if research using the donated samples leads to new and better tests or treatments for PSC in adults or autoimmune liver disease in children, you will not receive any form of compensation or payment. The study team will work with others in the public and private sector (e.g. the pharmaceutical industry) to successfully develop scientific discoveries for the benefit of all patients.

Participation in future studies

In the future, there will be other studies carried out by researchers who are not part of the current study. By looking at information stored in the research database, we may identify you as suitable to participate in one of these other studies. If so, your liver care team may contact you to ask whether you would like to take part in this other study. You would be provided with full information about this other study, and it would be your decision whether to participate in it.

If you decided not to participate in this other study, your decision would not affect your ongoing medical care. **If you do not want to hear about other studies taking place in the UK, please leave Box 15 on the consent form empty.**

What happens if I decide to withdraw from the study?

You are free to withdraw from the UK PSC Study at any time without giving a reason. If you choose to withdraw from the study, you will not be contacted by the study again. Please note this will not affect the care you receive from the NHS in any way.

You can withdraw from the study at one of two levels:

- **Withdrawal and data deletion** - this means that we will delete all of the data we hold about you, apart from your name, address, date of birth and NHS/CHI number. Your samples will also be destroyed. This approach prevents your information from contributing to future research. However it would not be possible to remove your data from research that had already taken place. We will make no further contact with you relating to UK PSC.
- **No further participation, but retain data** – this means that you consent for UK PSC to retain and use any data and samples already collected from you. This will enable us to study PSC and childhood autoimmune liver disease with the maximum number of study participants. We will make no further contact with you relating to UK PSC.

Please note that samples cannot be destroyed if they have already been prepared for testing.

If you wish to withdraw from the study, please contact the study team (Tel: 0121 371 8101; email ukpsc@uhb.nhs.uk).

What if something goes wrong?

We think it is unlikely that you will be harmed in this study. However, if you are harmed by taking

part in this study, owing to someone's negligence and provided the study protocol has been followed, then you may have grounds for legal action under the NHS Indemnity Scheme. If you suffer harm which is not the result of someone's negligence, there are no special compensation arrangements. Regardless of this, if you wish to complain, or have any concerns about the way you have been approached or treated during the course of this study, you should contact the study organizers. You can also contact the Patient Advice and Liaison Service (PALS) at the hospital you attend for your autoimmune liver disease.

Further information

If you would like further information, please visit the study website www.uk-psc.com. If you have any questions you can also contact the study Project Manager, <insert name> , (0121 371 8101 or email: ukpsc@uhb.nhs.uk).

Thank you for taking the time to read about the study. We realise that participation is voluntary and are very grateful to those who consider entering the study.

Yours faithfully,

A handwritten signature in black ink, appearing to read 'Palak Trivedi', with a long, sweeping horizontal stroke extending to the left.

Dr Palak Trivedi
Chief Investigator