Institute of Metabolism and Systems Research

University of Birmingham

B15 2TT

Dissecting Androgen excess and metabolic dysfunction – an Integrated Systems approach to Polycystic Ovary Syndrome through the assessment of detailed phenome and metabolome data

(The DAISy-PCOS Phenome study)

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Chief Investigators
Professor Wiebke Arlt
William Withering Professor of Medicine, Wellcome Investigator in Science
Institute of Metabolism and Systems Research
College of Medical and Dental Sciences, University of Birmingham

Study Sponsor
University of Birmingham
Research Governance and Ethics Manager
Room 119, Aston Webb Building
B15 2TT
researchgovernance@contacts.bham.ac.uk

Information Sheet for Prospective Participants

What is the purpose of the study?

Polycystic Ovary Syndrome (PCOS) affects 10% of all women, and it usually co-exists with high levels of male hormones (also termed androgens) and poor response to sugar-regulating hormones (also termed insulin resistance). Women with PCOS are at increased risk of metabolic complications such as diabetes, non-alcoholic fatty liver disease, high blood pressure and heart disease. However, very little is understood about how androgen excess and insulin resistance are linked and which patients have the highest risk of developing metabolic complications during their lives.

The main aims of the DAISy-PCOS Phenome study are to better understand metabolic risk in women with PCOS by examining the relationship between androgen excess and insulin resistance and looking for factors that identify those women who are at the highest chances of metabolic complications. The results of this research will help better understand the metabolic risk associated with PCOS and treat and, where possible, prevent the development of metabolic disease in affected women.

The DAISy-PCOS Phenome Study is a multi-centre study in the United Kingdom in Birmingham, Cardiff, Coventry, Dublin, Edinburgh, Leeds, and London. It is part of a more extensive PCOS research programme; thus, we will also use the study to help us identify women who may be suitable to participate in other PCOS-related clinical studies. We will provide you with more details on this during your study visit. Of course, it is entirely up to you to decide whether you want to participate in additional PCOS-related studies.

Do I have to take part?

You are under no obligation to participate in the study, and you would also be free to withdraw at any time without giving a reason, which will not prejudice your future care. To participate, you must be aged between 18-70 years and have a suspected diagnosis of PCOS. You cannot take part if you are pregnant, breastfeeding or taking any medication that affects the measurement of steroid hormones (e.g., glucocorticoids, contraceptives, etc.). If you are not sure whether you are taking such medication, we are happy to discuss it with you and clarify.

What should I do next?

Please read the following parts of this information sheet carefully as it will outline what will happen during the study. We will contact you to find out if you are interested in participating and will be happy to answer any questions; as per above, you are under no obligation to participate.

What will happen if I take part?

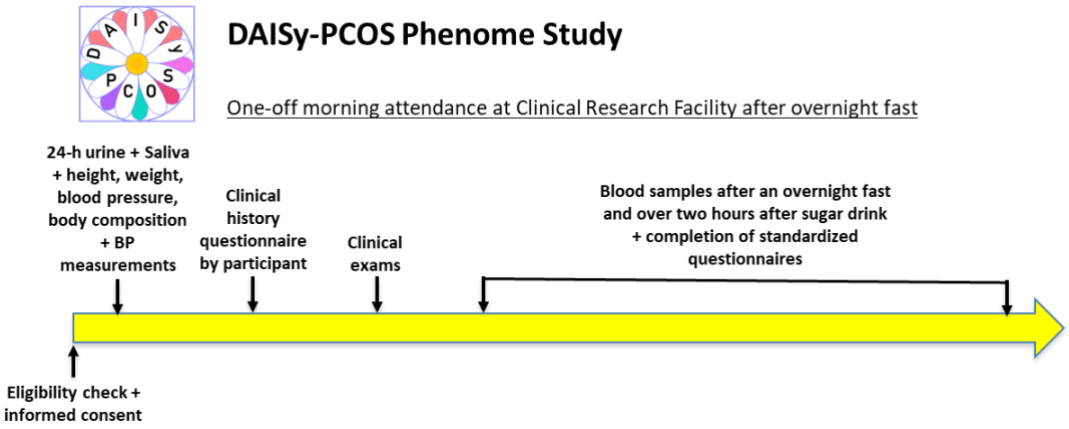
We will ask you to attend a single study visit, which will take place at the Birmingham NIHR/ Wellcome Trust Clinical Research Facility, Queen Elizabeth Hospital. The visit will last approximately 3-4 hours. You need to arrive in the morning in the fasted state (that means your last meal should not be later than 10 pm the previous day – sips of clear water permitted). We will ask you to collect 24-h urine during the day before your visit, and we will provide you with instructions for this.

On your visit, you will be asked to complete a questionnaire that will consist of questions about your medical, drug and family history. We will explain this in detail on the study day. These data will be stored in a cloud-based data server, which is secure and will only be accessible by the research team. We would discuss the study and procedures with you, check that you fulfil the required criteria (e.g., age) and make sure that there is nothing excluding you from the study – a brief medical history and physical examination alongside the questionnaire you will be filling in will confirm this.

Once we have confirmed your eligibility to participate in the study, we will measure your height, weight, waist circumference (your anthropomorphic measurements) and blood pressure. You will also undergo a body composition assessment using the bioimpedance technique, a specialised weighing scale that gives us an overview of the water and fat percentages in your body. We will then collect your saliva and blood samples. After collecting these blood samples, you will undergo a test called a 2-hour oral glucose tolerance test (2h-OGTT); It is a test used to determine whether your body has any difficulty processing sugar/carbohydrate. The steps for the 2-h OGTT are outlined below:

1. Your blood will be collected for measurement of glucose and insulin at the start of the 2h-OGTT, and this will be marked t = 0 min.
2. You will then be given a standardised sugar solution to drink within five minutes.
3. We will then be collecting blood at 30-minute intervals (t = 30, 60, 90 and 120 min); There will be no need for multiple needling into your blood vessels, as we will insert a line in your hand vein that will allow us to take multiple blood samples.

During the 2h-OGTT test, you will be provided with the standardised questionnaires related to PCOS to be filled in as part of this study. These questionnaires are associated with the impact of PCOS on mood, quality of life and sleep quality. This will be the end of the visit.



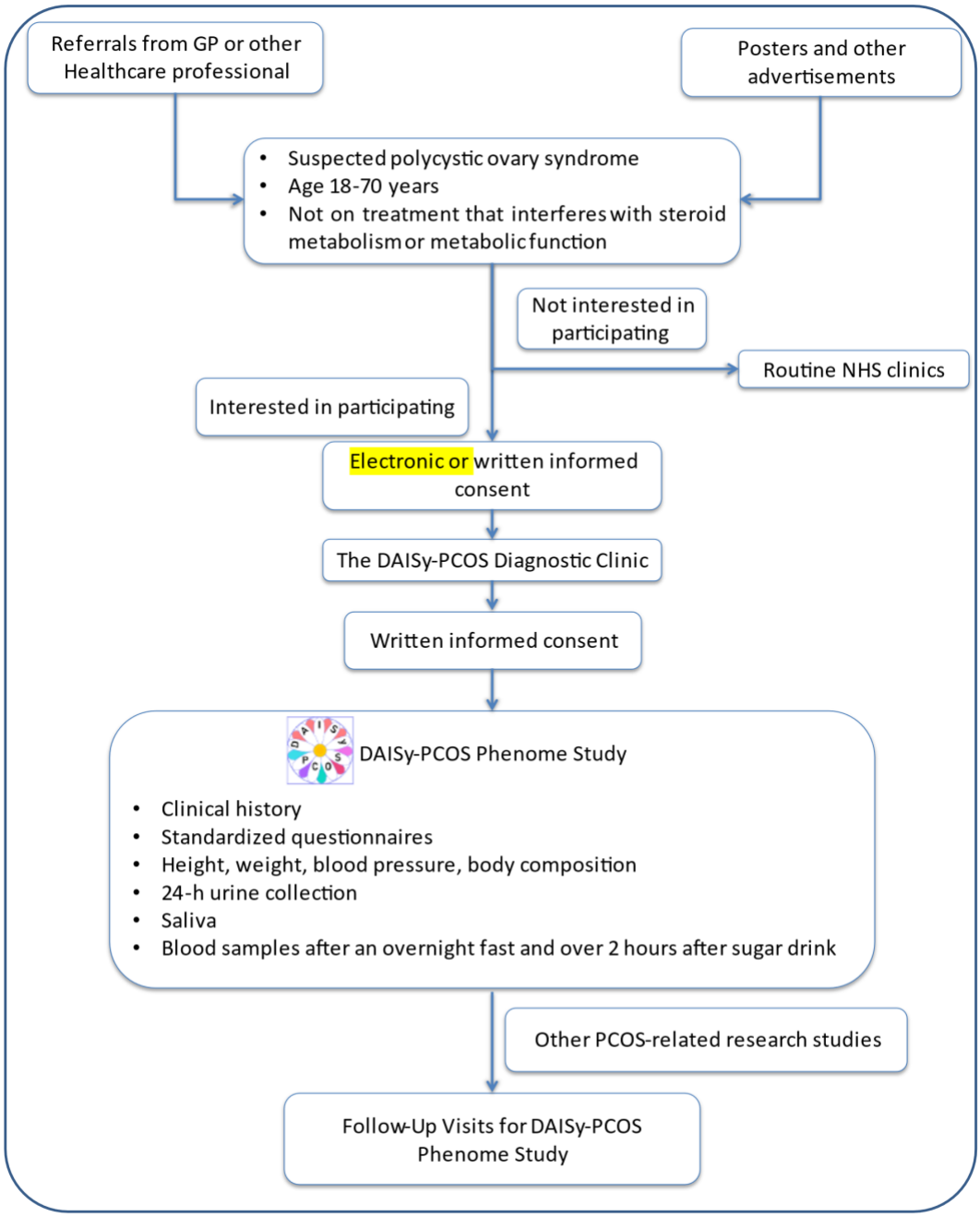
The blood, salivary, and urine samples are taken will be used to determine the concentration of metabolic and hormonal parameters. In addition, we will also store whole blood from you, with your consent, to have the opportunity to extract genomic DNA, i.e., your genetic information, at a later date. Though we do not plan genetic analysis in the first instance, having the possibility to analyse your DNA would allow us to match the hormonal and metabolic findings with genetic findings and, thereby, possibly further improve the new diagnostic and prediction tools we want to develop through the DAISy-PCOS Phenome study.

We might collaborate with other experts to analyse your blood and urine samples and your genetic information (blood only); this might include exchanging material with other Universities in the UK or other countries or with experts from the industry for use in ethically and scientifically approved research project.

These tests will be performed at the University of Birmingham and its affiliated facilities, including the University of Birmingham Steroid Metabolome Analysis Core and the Phenome Centre Birmingham.

We will also introduce you to a few closely related studies on the study day. If you are eligible, we will contact you, with your consent, later to check if you are interested in participating in one of those studies.

Women with PCOS can develop metabolic diseases such as type 2 diabetes and high blood pressure later in life, and we would like to keep track of you and check your health at regular intervals. Therefore, we plan to have future follow-up visits for all women participating in the DAISy-PCOS Phenome Study, which might happen in 3- or 5-year intervals. We will contact you and invite you to attend such follow-up study visits; you are not obliged to follow those if you would not like to do this.



What are the possible disadvantages and risks of taking part?

When taking blood samples: the blood sampling site might slightly bleed and bruise, there is a small risk of clotting and infection, but these will be minimised with good clinical practice and sterile techniques.

Blood volume taken would be a maximum of 88 mL, about 15 teaspoons (depending on the need for the oral glucose tolerance test). It is safe to lose this relatively small amount of blood during the study, and there are no adverse effects to expect from this procedure.

What are the possible benefits of taking part?

Although this study might not benefit you directly, the measurements taken during the study are part of "metabolic workup". In the long term, we hope that the information obtained from this study will lead to better understanding, diagnosis and management of PCOS. Any blood/urine results that come back out of the normal range will be sent to your GP and managed accordingly.

What if something goes wrong?

It is unlikely that something will go wrong, as this observational study does not involve any invasive intervention except for taking blood samples. If you are harmed, and this is due to someone's negligence, then you may have grounds for legal action for compensation against the sponsor of the trial, the University of Birmingham, or the NHS Trust, but you may have to pay your legal costs. NHS Trusts have a duty of care to patients treated, whether the patient is taking part in clinical research and the standard NHS complaints mechanisms will still be available to you (if appropriate).

Suppose you decide to complain about any aspect of the study at any point of the study. In that case, you can either contact the study investigators directly or contact the Patient Advice and Liason Service (PALS) at the Queen Elizabeth Hospital. PALS is located on Level 0 inside the main entrance of the Queen Elizabeth Hospital Birmingham. It is located to the left of the Information Desk, heading towards the Outpatients Department (opposite the Outpatient Pharmacy). Portal: https://www.uhb.nhs.uk/pals.htm; E-mail: PALS@uhb.nhs.uk or phone 0121 371 3280.

Alternatively, the point of contact for such instances would be the University of Birmingham Research Governance (Phone: 0121 415 8011, email: researchgovernance@contacts.bham.ac.uk), as the University of Birmingham is the Sponsor of the DAISy-PCOS Phenome Study.

What will happen to my data?

Personal data obtained from you during the study will be kept strictly confidential, handled, and stored according to the General Data Protection and Data Protection Act 2018.

Questionnaire data will be securely stored in a cloud-based electronic database which will be password secured and encrypted. This system is built on many years of experience from the team involved. Participants will only be identified using their unique participant number and year of birth.

Access to and use of the data will require authentication (password-based) and authorisation capabilities, respecting the data-sharing requirements of the partners involved. The default rule is that access is not granted to clinicians/researchers unless explicitly authorised by the study's Chief Investigator. All-access to and use of the system will be audited through log files that are automatically generated.

With your consent, samples you have given and the research data gathered will be stored for ten years by Professor Wiebke Arlt at IMSR for possible use in future ethically approved projects. No personal data will be kept or transmitted outside of the Queen Elizabeth Hospital Birmingham to use my samples for storage and future research.

If you consent to it, the researchers involved in DAISy-PCOS may, in the future, access electronic data from your central NHS records, for example, through NHS Digital. This will give researchers information routinely collected during your visits to your GP and hospital and let us find out about your health after the study has ended without contacting you further. To do this, we would send your name, gender, date of birth and NHS number with any request for information.

The system's security is governed by the policies of the University of Birmingham. The University's Data Protection Policy and the Conditions of Use of Computing and Network Facilities set out the security arrangements under which sensitive data should be processed and stored. All studies at UoB must be registered with the Data Protection Officer and data held by the General Data Protection Regulation and Data Protection Act 2018. The University have a designated Data Protection Officer, Mrs Carolyn Pike, OBE in Legal Services. The Study Centre has arrangements for the secure storage and processing of the study data that comply with UoB policies.
Data will be stored for at least 20 years. The University of Birmingham has standard hard copy and computer database legacy archiving processes. Archiving will be authorised by the University of Birmingham following submission of the end of the trial report. If you withdraw from the project, we will keep the information we have already obtained but, to safeguard your rights, we will use the minimum personally-identifiable information possible.

Your rights about your data. You might have the following rights in respect of your data:

- The right to access your data (often referred to as Subject Access Request)
- The right to rectification of inaccuracies in your data
- The right to erasure your information (in certain circumstances)
- The right to restrict processing of your data (in certain circumstances)
- The right to object to the processing of your data (in certain circumstances)
- The right to ask for your data to be transferred electronically to a third party.

However, your rights to access, change or move your information are limited, as we need to manage your data in specific ways for the research to be reliable and accurate. If you

withdraw from the project, we will keep the samples we have already obtained but, to safeguard your rights, we will delete all your personally identifiable information.

If you would like more information on your rights, would like to exercise any right or have any queries relating to our processing of your data, please contact:

The Information Compliance Manager, Legal Services, The University of Birmingham, Edgbaston, Birmingham B15 2TT
Email: dataprotection@contacts.bham.ac.uk Telephone: +44 (0)121 414 3916

If you wish to make a complaint about how your data has been processed, don't hesitate to contact our Data Protection Officer.

Nicola Cardenas Blanco, The Data Protection Officer, Legal Services, The University of Birmingham, Edgbaston, Birmingham B15 2TT
Email: dataprotection@contacts.bham.ac.uk Telephone: +44 (0)121 414 3916

You also have a right to complain to the Information Commissioner's Office (ICO) about how we process your data. You can make a complaint using the ICO's website.

Will my involvement in this study be kept confidential?

Yes. Participants will always be identified using their unique study identification number, date of birth, and initials. The study team will maintain the confidentiality of all participant data and will not disclose information by which participants may be identified to any third party. This is except for those directly involved in the participant's treatment and regulatory organisations for which the participant has given explicit consent for data to be shared across. We will also notify your GP that you intend to participate in this study with your permission.

What will happen to the results of the research study?

We will notify you when the study results are published. They will be given to the participants by using a participant newsletter, the information provided by collaborating patient charities, and the trial website.

Who is funding the study? Who has reviewed the study?

The Wellcome Trust funds the study as part of a Wellcome Trust Investigator Award in Science to the Chief Investigator, Professor Wiebke Arlt. The University of Birmingham acts as the sponsor of the study. The study has been reviewed and approved by 19/WM/0110**.**

We have also discussed the study design with ten patients with PCOS and a group of women with PCOS who will also be giving ongoing feedback about this research.

Expenses and Payments

If you participate, you will receive volunteer compensation to cover reasonable travel expenses (parking fees, public transport).

I am interested in participating – What should I do next?

If you are interested in participating, please contact the following email address: daisy-pcos@contacts.bham.ac.uk, or text/WhatsApp 07825112102.

In addition, we will also follow up on the invitation letter to find out whether you want to participate.