

General Health Outcomes in Subfertile Men: a UK register-based cohort study

What are we trying to do?

This is a large study of men with known subfertility (identified through the Human Fertilisation and Embryology Authority (HFEA) registers of couples undergoing assisted reproduction treatments in UK clinics). The aim of the study is to compare long-term cancer and other health outcomes of these subfertile men with similar men who have not sought assisted reproduction treatment for the conception of a child.

Why are we doing this?

Fertility rates in the UK since the turn of the century have been decreasing and a growing number of individuals have sought assisted reproductive technology (ART) treatment for the conception of a child. Male subfertility (known as any form of reduced fertility with prolonged time to conception) affects about half of all couples undergoing fertility treatments. ART substantially increases the chances for the affected men to become fathers, but the effects of the underlying fertility problems on their health remain unclear.

We would like to understand the impact of subfertility on short and long-term cancer and other health outcomes of men. The results of this research will provide critical insight into the sequelae of subfertility, help develop targeted interventions, advance current diagnosis, and treatment methodologies. This is possible in the UK as we have electronic NHS health records and reporting of all cycles of assisted reproductive therapy undertaken in the UK to the HFEA is a legal requirement.

Who is doing this study?

The study is led by Professor Alastair Sutcliffe, Professor in General Paediatrics, based at the Institute of Child Health at University College London. The study team includes Julian Gardiner, Mitana Purkayastha, Faiza Afzal, and Darina Peycheva. You can find out more about the study team [here](#).

How will we do this?

We will use information about all men identified through couples who underwent fertility treatment in the UK between August 1991 and September 2009 for male factor subfertility and match them with men of a similar age who have not sought ART for the conception of a child. We will look at cancer and non-cancer health outcomes, as well as early death, of around 160,000 men who underwent ART and compare them to approximately 320,000 men from the general population (matched controls). We will get this information from:

- Records of fertility assessment and treatments held by the Human Fertilization & Embryology Authority. The information includes patient's diagnoses (such as

type and cause of subfertility) and treatments, as well as outcomes of the treatments (such as conceptions and births).

- Records of hospital care, cancer, and mortality held by NHS Digital. The information includes admissions or appointments at hospital (such as dates of admission, discharge or attendance, diagnoses and treatments, and specific conditions (such as cancer or heart disease). It also includes information about cause of death.

To access hospital care, cancer, and mortality data for the subfertile men in the study, HFEA will securely share with NHS Digital the minimum amount of identifiable data for them. This will include sex, name, date of birth, town/district and country at birth, and NHS number (if available). No fertility assessment or treatment data will be shared with NHS Digital.

NHS Digital will use this information to identify and extract the available hospital care, cancer, and mortality information for the affected men, as well as to identify men with similar characteristics from the general population (as a control group for our analysis) and extract their data too.

HFEA and NHS Digital work under strict data security regulations and have a lot of experience with records linkage studies using patient data and keeping patients' data secure.

Before our research team can access information from NHS Digital, any information that could be used to identify men, such as their NHS number, their name, full date of birth or postcode, will be removed. This means that the information will be de-identified by NHS Digital and researchers will not have access to identifiable information about the men included in this study.

HFEA will also securely share with our research team de-identified fertility assessment and treatment information for the subfertile men. Neither this information will include details that allow individuals to be identified. At no point will our research team have access to identifiable information about the men included in this study.

Our research team will combine these two sources of data (fertility assessment and treatment and hospital care, cancer, and mortality) together using a unique study member number. We will use this information to find out whether men affected by subfertility are at greater risk for adverse health compared to men from the general population. Further information about processing this information is outlined below.

The 'data controller' under the General Data Protection Regulation (GDPR) is responsible for what happens to this information. The data controller for the data analysed in this study is University College London. Find out more about how we handle personal information for this study in the [UCL research participants privacy notice](#) or email Professor Alastair Sutcliffe (a.sutcliffe@ucl.ac.uk).

How do you know if you have been included in this study?

Any man on the database of NHS patients may be included in this study (unless you have specifically asked not to be). This is because men identified through HFEA registers of couples undergoing assisted reproduction treatment in UK clinics between August 1991 and September 2009 may be linked to any men on the NHS database of patients with similar characteristics such as age, number of children, and geographic region they live in. However, the research team cannot tell you if your information is included in this study as we do not have any names to allow us to identify individuals. Further information about opting out of research is outlined below.

Can I choose whether to take part in the study?

No, this is not possible. The study will include around 500,000 men (160,000 men identified through HFEA registers of couples undergoing assisted reproduction treatment in UK clinics between August 1991 and September 2009 and approximately 320,000 men from the general population with similar characteristics as matched controls). Moreover, our research team will not have any identifiable information for the men included in this study such as contact details, so it would not be possible for us to contact them individually to ask if we can use their information. Therefore, we seek support under Regulation 5 of the Control of Patient Information (COPI) Regulations ('s251 support') for special permission to access these records without consent. Section 251 of the NHS Act 2006 allows the use of confidential patient information for medical research when it is not possible to use anonymised information or when seeking consent is not practical.

Can I opt out of being included?

If you are included in the study dataset because you and your partner underwent fertility treatment for male factor subfertility before September 2009 and your information is held on the HFEA register of fertility treatments, you can opt out of this study until 1st July 2023 by contacting Professor Alastair Sutcliffe (a.sutcliffe@ucl.ac.uk) or the HFEA (register@hfea.gov.uk). Anyone can opt out of their patient information being shared for research purposes through the NHS website or by speaking to your GP. More information about the NHS and your data can be found at <https://www.nhs.uk/your-nhs-data-matters/>. If you have opted out of data sharing **before** the study data linkage begins your data **will not be included in this study**. Once the study team receives the data, we will not be able to identify individual men because all identifiable information will have been removed. This means the study team will be unable to exclude men at this point. For more information about data sharing and the national opt-out please visit the Human Fertilization & Embryology Authority and NHS Digital websites.

What will happen to the results?

The study results will be published in peer-reviewed scientific journals and presented at national and international academic and practitioner-led conferences as well as meetings primarily aimed at patients and families. Outputs will also be distributed via

the UCL and the study websites and partner organisations including NHS England's Fertility Treatments Advisory Group (which makes recommendations to the UK government on implementing strategy in the devolved administrations), Fertility Network UK and All About Fertility (the nation's leading patient-focused fertility charities providing support and advice to anyone affected by fertility issues), Human Fertility & Embryology Authority (responsible for regulating all fertility treatment cycles in the UK), British Fertility Society.

Will we share participant data?

The de-anonymised dataset (where person identifiable information is removed) will not be shared with other researchers or third parties. The dataset will be stored in a secure location and access to it restricted to named individuals from our research team.

How will we keep participant data secure?

We will keep the information secure in the UCL's Data Safe Haven. The UCL Data Safe Haven (DSH) is a technical solution for storing, handling, and analysing sensitive data. It has been certified to the ISO27001 information security standard and conforms to the NHS Digital's Data Security and Protection Toolkit (DSP Toolkit). This demonstrates that we have high standards for keeping participant data secure.

How long will we keep the data for?

Once the study is completed, the data will be stored for a period of 10 years, after which it will be securely destroyed, in accordance with the [UCL records retention schedule](#).

To better understand the long-term health of subfertile men, it is important that we follow these men throughout their lifespan, and that this linkage is extended in the future to ensure long-term follow-up. For this purpose, a data file of identifiable information for the men involved in this study will be securely held by HFEA and NHS Digital for future use.

Who is funding this study?

The study is funded by the [Wellcome Trust](#). The Wellcome Trust is a charitable foundation focused on health research.

Who can I contact for more information?

Please contact Professor Alastair Sutcliffe for further information (a.sutcliffe@ucl.ac.uk).

Complaints

To make a complaint about how we have handled personal data you can contact our Data Protection Officer (data-protection@ucl.ac.uk) who will investigate. You can also

make a complaint with the Information Commissioner's Office (ICO) if our response is not satisfactory.