FUNDED BY NIHR | National Institute for Health and Care Research

Birmingham Clinical Trials Unit

PRINT ON FERTILITY CENTRE HEADED PAPER

The UNiTY Trial: A randomised controlled trial evaluating the clinical and cost effectiveness of IVF versus IUI for UNexplained InfertiliTY

COUPLE INFORMATION SHEET AND INFORMED CONSENT FORM

We invite you to take part in a research study: The UNiTY Trial

Before you decide to take part, it is important for you to understand why the research is being done and what it will involve.

- Please take time to read the following information carefully and discuss it with your GP, friends and relatives if you wish.
- It is entirely your choice whether or not to take part in this research study. If you decide not to take part, this will not affect the care you are receiving from your doctors.
- Ask us if there is anything that is not clear or if you would like more information.

Thank you for reading this information. If you decide to take part you will be given a copy of this information sheet and your signed consent form.

Important things that you need to know

- We want to find the best way to help couples with unexplained infertility to have a child.
- We are comparing whether it is better for couples to undergo 1 cycle of IVF (In-Vitro Fertilisation) treatment or 3 cycles of IUI (Intrauterine Insemination) treatment. We will then compare both the success and costs of these treatments.
- Regardless of which treatment group you are in, you will receive the usual follow-up care from the Fertility team.
- Being part of the study will decide which treatment you are given, but it will not change how you receive that treatment.
- You can stop taking part in the study at any time, without giving a reason. Your original treatment and care plan will not be affected in any way.

How to contact us

If you have any questions about this study, please talk to your doctor or another member of your clinical team:

Local Principal Investigator:
[INSERT NAME]
Local Research Nurse/Midwife:
[INSERT NAME]
Telephone number:
[INSERT NAME]
Email Address:
[INSERT NAME]

unity@trials.bham.ac.uk
www.birmingham.ac.uk/unity

1 Background

One third of all couples with a fertility issue have a diagnosis of unexplained infertility, with no clear reason for their problem conceiving identified despite tests. This has a major emotional impact and results in couples considering in vitro fertilisation (IVF).

In a normal monthly cycle usually only one egg develops to a stage where it may be fertilised by sperm to form an embryo (earliest stage of a baby). IVF treatment involves daily self-injection of hormones to boost the egg supply. This is monitored with vaginal ultrasound scanning. Eggs

are collected by passing a needle through the vaginal wall into the ovaries. The eggs are mixed with the sperm to achieve fertilisation before they are transferred back into the womb days later.

Intrauterine insemination (IUI) is simpler with a much lower dose of hormones. Sperm are prepared in the laboratory before being introduced directly into the womb. This increases the chance of fertilising the egg. European guidance recommends IUI for couples with unexplained infertility, however it is not routine treatment in the UK.

To answer the question of which approach is best for unexplained infertility we would like to carry out a study called a randomised controlled trial where couples (NHS or Private) will be randomly allocated to either three cycles of IUI or directly to an IVF cycle. Those couples having IUI first, if unsuccessful, will still be able to follow through to IVF, which will be NHS funded if they are eligible.

Alongside the treatment trial, we may ask you how you feel about each treatment option; this will not change the treatment you are offered. This is an optional sub-study in which we will interview you about other things such as quality of life, work disruption, and emotional/physical burden. A separate information sheet and consent form is available for this study.

You have been invited to take part in this study because as a couple you have been diagnosed with unexplained infertility (UEI) and your fertility care team has therefore recommended that you undergo IVF treatment to help you conceive.

The study is taking place in at least 11 Fertility Centres across the UK and plans to recruit 942 couples.

2 What will happen if we take part?

By taking part in this trial, you will either have your standard single IVF treatment, unchanged and as suggested by your care team, or up to three IUI treatments.

Neither you nor your doctor or nurse will be able to choose which treatment you receive. Your treatment will be decided by a computer at the UNiTY Trial Office. The computer will allocate the treatment randomly. You will have an equal chance of receiving either 3 cycles of IUI or 1 cycle of IVF. This method of research is called a “randomised controlled trial”.

Do we have to take part?

Participation in our study is entirely voluntary. If you decide to take part, we will check you are eligible and you will be asked to sign a consent form. If you do not wish to take part, you will not have to give a reason and your decision will not affect the care you will receive. Similarly, if you do decide to take part, you will be able to withdraw from the study at any time and without giving a reason, and without any effect on your original care plan.

What will we need to do?

The study does not require you to do anything additional to the treatment plan that your fertility care team will discuss with you. We will follow the outcome of your treatment using routine data collected by all treatment centres. The Human Fertilisation Embryology Authority (HFEA) legally require information about the outcome of your pregnancy irrespective of you being in the trial or not. This data is also essential for our research.

Analysis of sperm samples

We will also ask for your permission to take videos of your sperm sample that is used in your treatment as well as some microscope slides with stained sperm fixed to them. This will not affect the sperm that is used for your treatment. Because of the way they are prepared, samples you provide will never be used for someone else’s treatment.

We hope to use these samples as part of a sub-study to ensure all Fertility Centres are assessing sperm in the same way, and to better understand how sperm properties contribute to the success of treatment. This may help us better diagnose and assign patients to certain treatment in the future. These videos and microscope slides will be labelled with a unique number that the researchers cannot

use to identify you. The same videos will be taken regardless of the trial group you were entered into.

The laboratories will handle your videos and microscope slides with the same duty of confidentiality as they would for any clinical sample. The videos and microscope slides will be transferred to the University of Birmingham, and stored securely for a minimum of 30 years as advised by the Royal College of Pathologists. The University of Birmingham will have overall control over what happens to the videos and microscope slides.

3 Is it safe?

Yes, we are only testing established procedures. Both IVF and IUI have been extensively tested and have been used within the UK and worldwide. Your treatment will remain the same as in standard practice guidelines, as will the way your treatment is followed up afterwards.

What if new information becomes available?

Sometimes new information about treatments becomes available. If this happens, we will tell you and discuss whether you should continue in the study. If you decide not to carry on with the study then we will make arrangements for your care to return to standard care. If you decide to continue in the study then we may ask you to sign an updated consent form. If the study is stopped for any other reason, we will tell you and arrange your continuing care.

What are the risks?

IVF is routinely performed in the UK, and IUI is well established and is routinely performed in many countries around the world. There are no other trial-specific risks beyond those such as multiple births that were explained in the information that you had before treatment. You will sign routine local treatment consent forms as would any couple beginning fertility treatment.

4 What are the possible benefits of taking part and will the research study have any significance to us?

If you are allocated to the IUI treatment you will get up to three cycles of IUI before progressing on to your originally suggested IVF treatment.

If you are allocated to the IVF treatment, being part of the study will not change your chances of having a baby.

In either case, you will be taking part in research which may change how we routinely treat couples like yourselves with unexplained infertility.

We are self-funding our treatment, can we still take part?

Yes. As a self-funding couple you will be asked to pay up-front for your IVF cycle before you are entered into the trial. If you are then allocated to the IUI treatment, and are successful in achieving a live birth, you will be refunded your up-front payment, otherwise it will be expected that you go on to have IVF as planned using the fee that you have already paid.

5 What happens to the information you collect about us?

How will information about us be collected?

We will need to use information from you and from your medical records for this research project, and if you have a baby during the trial then we would also like to have access to their records.

This information will include your:

- Name
- Contact details
- Date of birth
- NHS Number

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

We will keep all information about you and your baby safe and secure.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will collect our study information from your hospital notes and as part of any discussion with the care team. We will ask that you complete a short quality of life questionnaire around your first visit and at approximately 8 and 18 months.

We would also like to contact you after your participation in the study has ended to ask your permission to follow you up in the long term.

What data is recorded about us for the study?

If you agree to take part in the study we shall:

- Collect some general data and medical history about both of you,
- Ask about your medical history including any gynaecological disorders and surgical operations of the partner providing eggs,
- Ask about any previous pregnancies and their outcome,
- Record the level of female hormones and assess the semen profile, which are both routinely measured as part of fertility assessment before IVF procedures,
- Record the outcome of the pregnancy.

Will our taking part be kept confidential?

Yes, if you decide to participate in the UNiTY Trial, the information collected about you (and your baby if you become pregnant during the trial) will be handled strictly in accordance with the consent you have given and the Data Protection Act 2018.

More information on how the University processes personal data can be found on the University's website on the page called 'Data Protection - How the University Uses Your Data' (https://www.birmingham.ac.uk/research/bctu/data-protection.aspx).

The University of Birmingham, Edgbaston, Birmingham B15 2TT is the data controller for the personal data that we process in relation to you.

Informing your General Practitioner

It is expected that we tell your GP of your participation in UNiTY, and we will ask for your consent to do this. All information about you and your treatment will remain confidential.

How will my personal data be kept secure?

The University takes great care to ensure that personal data is handled, stored and disposed of confidentially and securely. Our staff receive regular data protection training, and the University has put in place organisational and technical measures so that personal data is processed in accordance with the data protection principles set out in data protection law.

The University has an Information Security Management System covering the protection of personal information. In relation to this project, electronic data will be kept on secure, encrypted IT servers within the University of Birmingham and also securely stored on a trusted external database provider, REDCap. Any physical paperwork containing identifiable data will be kept in an access-controlled, secured room inside a locked filing cabinet at all times.

How long will my personal data be kept?

Your data will be retained for 10 years after the publication of the research outcomes. 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.

What are your choices about how your information is used?

- You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

- If you choose to stop taking part in the study, we would like to continue collecting information about your health from your fertility clinic. If you do not want this to happen, tell us and we will stop.
- We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you.
- If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

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 personal 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 is being or has been processed, please contact our Data Protection Officer:

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 the way in which we process your personal data. You can make a complaint using the ICO's website https://ico.org.uk

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team, or
- by sending an email to unity@trials.bham.ac.uk

7 What do I do if I have any concerns?

What if there is a problem?

If you experience any adverse consequences of treatment, then please contact your local Clinical Lead: INSERT CONTACT DETAILS HERE

Any complaint about the way you have been dealt with or any possible harm you may have suffered should be addressed to the HFEA Person Responsible at your clinic: INSERT HFEA PR Name and contact phone number.

If you are being treated with NHS funding (or are privately-funded and receiving treatment at an NHS centre), remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. NHS Direct can advise on NHS complaints on 111. Independent advice or support can be accessed by contacting the Patient Advisory Liaison Service (PALS) [ADD LOCAL PALS CONTACT DETAILS].

If you are self-funded and receiving treatment at a private healthcare centre, remain unhappy and wish to complain formally, you can do this directly through the healthcare provider [ADD CONTACT DETAILS OF LOCAL COMPLAINTS OFFICE].

If you have a concern about any research aspect of this study, you should contact the Trial Coordinator on the contact details at the end of this leaflet.

If you have private medical insurance, you should tell your insurer that you are taking part in research. They will let you know directly if it affects your policy.

The Sponsor (University of Birmingham) has insurance in place for the duration of the research project including legal liability cover.

What will happen if I don't want to carry on with the study?

You may choose to withdraw at any time, without giving a reason. Your decision will not affect your original treatment plan, however if you were allocated to IUI treatment you will not be able to start any remaining cycles of IUI. You should contact your doctor or a member of the clinical team if you change your mind and decide that you no longer want to take part and you will be asked to complete a withdrawal form.

At the end of the study your data will be archived in line with Research Governance Framework guidelines and Trust policy of each participating centre.

8 More information about taking part

Who is organising and funding the research?

This study has been funded by the National Institute for Health Research (NIHR). It is organised, managed and coordinated by the University of Birmingham, and data will be collected and stored by this institution. The study is also sponsored by the University of Birmingham.

Do we have any rights to the research?

Taking part in this project will not give you any rights to the research. In the event that the results of certain parts of the research are patented and have commercial potential, you will not receive any financial benefit from this.

What will happen to the results of the study?

When the results of the study are known, we will inform you of the overall findings by email and/or via our website. We will also publish the overall findings of the study in medical journal(s), for consideration by the National Institute for Health and Care Excellence (NICE).

Who has reviewed the study?

To have obtained funding from the NIHR, the study had to go through review by experts who felt this study to be of relevance and importance to couples undergoing treatment for Unexplained Infertility. The study has received a favourable opinion from the East Midlands - Derby Research Ethics Committee. The Data Monitoring and Ethics Committee (DMEC) and Trial Steering Committee (TSC) will be supervising the study data on a regular basis.

9 Where can I get more information?

If you have any **specific queries** regarding your fertility treatment or eligibility to the study, please contact your local Research Team on the contact details on the front page. They will answer any questions you may have and arrange to discuss the project further with you in the clinic when you attend for your next consultation.

With any **general queries** regarding this study, you may also contact the Trial Coordinator via: unity@trials.bham.ac.uk

www.birmingham.ac.uk/UNITY

The UK Clinical Research Collaboration has produced a guide entitled, 'Understanding Clinical Trials'. This can be downloaded from their website: UKCRC | UK Clinical Research Collaboration and could be useful if you require general information about research.

Association of Research Ethics Committees (AREC) is an independent, self-governing body which promotes excellence in ethical research in human beings. It publishes a leaflet entitled 'Medical Research and You'. This leaflet gives more information about medical research and looks at some questions you may want to ask. A copy is free to download from their website www.arec.org.uk

Another source of independent advice or support is the Patient Advisory Liaison Service (PALS). For more information on PALS or to find your nearest office visit their website at What is PALS (Patient Advice and Liaison Service)? - NHS (www.nhs.uk) or ask your doctor.
If you would like further support, you can contact the local fertility counselling service based at your healthcare provider on [INSERT LOCAL FERTILITY COUNSELLING SERVICE DETAILS].

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Couple Trial ID: | | | | | / | | | | |

(to be completed by research staff)

THE UNiTY TRIAL: COUPLE INFORMED CONSENT FORM: Please complete one form per individual:

Chief Investigator: Professor Jackson C Kirkman-Brown.
Principal Investigator: XXXXXXXXXX

	Initial each box to confirm consent
1. I confirm that I have read and understand the patient information leaflet (version 2.0, dated 17 January 2024) for the UNiTY trial. I have had the opportunity to ask questions, and these have been answered satisfactorily.	
2. I understand that my participation in the trial is voluntary, and I am free to withdraw at any time without my treatment or legal rights being affected.	
3. I understand that a copy of my consent form, which identifies me by my name, and personal information about my progress, will be sent in confidence, to the study organisers at the University of Birmingham where my data will be stored for the UNiTY Trial. I agree to the transfer and storage of this data.	
4. I understand that all information collected on me, and my baby/babies (if applicable), for this study will be subject to the General Data Protection Regulation and Data Protection Act 2018. This information will be stored securely at the University of Birmingham that is acting as the Data Controller for the UNiTY trial. I understand that I can withdraw my consent for the University of Birmingham to process the data about me at any time.	
5. I understand that the information collected on me, and my baby/babies (if applicable) will be used for medical research only and that I will not be identified in any way in the analysis and reporting of the results. I understand that even if I withdraw from the study, information already collected about me and my baby/babies (if applicable) may be included in the final study analysis after being anonymised.	
6. I understand that relevant sections of my medical notes and those of my baby/babies if applicable (both paper and electronic) and data collected during the study may be looked at by individuals from the research team, representatives of the sponsor, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research and any future related follow-on studies. I give permission for these individuals to have direct access to my records.	
7. **Partner providing sperm only -** I understand that videos of my sperm sample and fixed (dead) sperm surplus to our treatment will be taken and used for quality control to investigate male diagnosis in unexplained infertility.	
8. I understand that the information held by my fertility treatment centre may be used to keep in touch with me and follow up my status for the purposes of the study.	
9. I understand that researchers for the UNiTY Trial based at my hospital or at the University of Birmingham may contact me by telephone, mobile telephone, post or e-mail to request information. Where this relates to unexplained infertility related studies, my updated contact details may be traced through NHS databases and GP records.	
10. I understand that my General Practitioner will be informed about my participation in this trial.	
11. I understand the information that I have been given about the UNiTY trial and I agree to take part.	

Name of Participant: _____ **Date:** _____ **Signature:** _____

Name of Researcher: _____ **Date:** _____ **Signature:** _____

For the translator (if required): *I confirm that I have interpreted the study information to the best of my ability and ensured the patient fully understands everything that has been given to them to read/verbally explained to them*

Name of translator: _____ **Date:** _____ **Signature:** _____

Master copy for Site File, 1 copy for participant notes, 1 copy for Participants, 1 copy for UNiTY Trial Office