Participant Information Leaflet

Gx Media Study

A sibling oocyte study to investigate the impact of gamete preparation, insemination, and embryo culture media supplemented with antioxidants on clinical outcomes following fertility treatment.

Invitation

We are inviting women and male partners attending the Hewitt Fertility Centre (HFC), whose treatment plan involves In Vitro Fertilisation (IVF) or Intracytoplasmic sperm Injection (ICSI) using their own gametes (eggs and sperm) to take part in a research study. The Gx Media Study will involve introducing cell culture media within the laboratory process which has been supplemented with additional antioxidant properties to evaluate the effect this has on treatment outcomes when compared to the non-supplemented media which is currently used within the HFC laboratory.

Before you decide whether or not to take part it is important to understand why the research is being performed and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish. A member of the research team will go through the information with you and answer any questions you may have.

Please take time to consider this information before you decide whether or not you wish to take part.

Thank you for reading this.

What is the purpose of the study?

During the laboratory portion of fertility treatment your gametes (eggs / sperm) and embryos are exposed to stressors that they would not normally experience in the uterus. One of these stressors is called oxidative stress, which occurs due to an imbalance between the production and build-up of a compound called reactive oxygen species (ROS).
In the follicle (egg), semen (sperm), and uterus (embryo), cells are protected from oxidative stress by naturally occurring antioxidant compounds which reduce the damaging effects of ROS. In the laboratory, sperm cells are removed from the semen and eggs from the follicular fluid and are temporarily placed in a dish containing a type of sterile fluid called 'media'. This special formula contains all the nutrients and compounds fertilized eggs need to develop into embryos.

The media which is currently used within the HFC laboratory does not contain any additional antioxidants therefore gametes and embryos may have less protection against oxidative stress.

The manufacturer of the culture media we currently use at the HFC laboratory have developed a supplemented formula which contains the exact same properties as products currently used, with the inclusion of three additional antioxidants: Alpha-lipoic acid (ALA), acetyl-L-carnitine (ALC) and N-acetyl-L-cysteine (NAC).
This antioxidant containing media is CE marked and commercially available for use within fertility treatment centres both nationally and internationally. We would like to know more about the potential benefits of this media and whether our patients would benefit from having their treatment using it.

Why have I been invited to take part?

We are inviting all female and male partners aged 18 or over who are undergoing fertility treatment at the HFC to take part in the Gx Media Study. You have been invited as your treatment plan includes IVF / ICSI using non-donated gametes (treatment using your own egg and sperm cells). As this research study involves both gametes and is looking at fertility treatment outcomes, we will invite both female and male partners to take part as a couple. It would not be possible to take part on an individual basis or if your treatment plan includes using donated eggs or sperm.

What does participation involve?

If you and your partner agree to take part in the Gx Media study, we will ask you both to provide full informed consent before your treatment begins by signing an informed consent form.

A research specific informed consent consultation will be arranged with a member of the Gx Media study team. This appointment will take place at the Hewitt Fertility Centre (HFC) within Liverpool Women's NHS Foundation Trust and take approximately 20 minutes.

To reduce inconvenience or burden of additional hospital visits, informed consent can be arranged to align with any scheduled visits you may have, leading up to the beginning of your treatment. Alternatively, a research visit can be arranged at your convenience if preferred.

During the consent conversation, a member of the research team will discuss the study with you both and answer any questions you may have. If you would like to take part, the researcher will ask you both to sign an informed consent form. This consent form will also be signed by the researcher, a copy will be filed in your clinical records, and you will be given a copy to keep for your own records.

Your active participation in the Gx Media Study will begin on the date you and your partner sign the informed consent form and end on the day your treatment cycle is completed (the day your embryos are transferred and/or frozen). While your active participation will end at this point, we will continue to monitor your medical records to collect routine clinical information or 'data' relating to your fertility treatment and associated clinical outcomes.

The Gx Media Study is primarily a laboratory based scientific study therefore participation does not alter your prescribed treatment plan or involve any additional hospital visits. All samples will be handled, processed, and stored in accordance with stringent HFC standard operating procedures and laboratory protocols. All samples will be handled with the same level of care than if you chose not to take part in the study.

What does study involve as a couple?

Consent will be sought for the preparation of both partners gametes and culture of any resultant embryos to be separated into two groups. Half will be prepared / cultured using the standard media currently used within the HFC Laboratory. The other half will be prepared / cultured using the formula which has been supplemented with additional antioxidant properties.

Following embryo transfer, the research team will collect some routine data from your clinical records, this will include basic information related to your treatment and fertility treatment outcomes. The data we will be monitoring and analysing are:

• Age at time of participation of study • Ethnicity • BMI • Cause of infertility • Previous treatment outcomes • Semen analysis results pre and post preparation • Oxidative stress measured in the sperm ejaculate and lead follicular fluid before gamete preparation	• Number of eggs collected • Number of eggs fertilised • Embryo development timelines • Quality of embryos at day 3 (embryo grade) • Quality of embryos at day 5 (embryo grade) • Number of embryos transferred or frozen. • Positive pregnancy test rate • Clinical pregnancy rate • Biochemical pregnancy rate

We will also seek your permission to view time-lapse images recorded for monitoring purposes during your embryo's development.

Female Participant

On the day of egg collection your eggs will be collected in line with standard of care policy and procedures and as per your prescribed treatment plan. Once transferred to the HFC laboratory your eggs will be separated into two groups; one half will be prepared in standard media and the other half prepared using media supplemented with antioxidants.

During egg collection fluid will be drained from follicles on the surface of your ovaries which contains your eggs. Once the HFC laboratory have separated these eggs from the fluid, they will take a small sample of fluid to test for oxidative stress. This procedure would not occur if you were not participating in the Gx Media Study, and we will seek your informed consent to perform this test.

Once your eggs have been prepared and fertilized using your partners sperm, they will be placed the same culture media assigned at the above egg collection stage.

Male Participant

On the day of egg collection, you will be asked to produce a semen sample as part of your prescribed treatment plan. Once this sample has been transferred to the HFC laboratory a small sample of this will be used to test for oxidative stress. This procedure would not occur if you were not participating in the Gx Media study, and we will seek your informed consent to perform this test.

Your semen sample will be processed, and sperm separated into two groups; one half will be prepared in standard media and the other half prepared using media supplemented with antioxidants.

Following this, your sperm will be used to fertilize your partners eggs in accordance with your prescribed treatment plan. Fertilised eggs will then be placed in the same culture media that was assigned at the above sperm preparation stage.

Do I have to take part?

No, you do not have to take part. You can choose whether you would like to take part or not. If you agree to take part now, you can choose to stop or withdraw at any time. If you decide to withdraw or not take part this will not affect the standard or method of care, you receive from your clinical team in future in any way. Before making any decisions, please take the time to read this information leaflet carefully and discuss any questions you have with the research team.

What should I do if I want to take part?

If you and your partner decide you would both like to participate in the Gx Media Study or would like more information, please discuss this with a member of your clinical team who will be able to assist. Alternatively, please contact the research team directly using the contact details provided at the end of this information leaflet.

What happens if there is not enough sperm or eggs on the day of treatment?

In the event less than six eggs are collected or there is insufficient volume of semen on the day of treatment, you would not continue in the Gx Media Study for that individual treatment cycle. Your gametes and embryos would be treated using our current standard culture media. Six has been set as the minimum egg number needed as this allows us to account for the variation in egg quality and produce more reliable results. Due to the increased handling of your gametes during the study, if we collect fewer than 6 eggs we will prioritise standard care for you. A member of the research team would discuss this with you, and you would be free to take part in any future treatment cycles. The research team would go through the consent procedure with you again prior to further treatment cycles. This study will close to recruitment on 31-12-2025 or once the necessary number of participants (166) has been reached, which ever comes first; Therefore it may not be possible to take part if your future treatment cycle occurs after the study has ended.

What will happen if I do not take part?

If you decide not to take part or choose to withdraw your participation this will not affect the standard or method of care you receive in anyway. Participation in this research study is entirely voluntary, therefore if you choose not to take part you will continue to receive the best possible care. We would like to thank you for taking the time to consider this information and wish you well on your fertility journey.

Due to the nature of the study, withdrawal from participation is only possible prior to egg collection if you do not want the antioxidant supplemented media to be used at all. Withdrawal at a later stage is possible, however this would introduce extra gamete and embryo handling as they would need to be removed from their controlled environments. If you choose to withdraw from the study, your treatment will follow standard care as stated in your treatment plan.
To withdraw from the study Please contact Chief Investigator: Bijal.patel@lwh.nhs.uk

What are the possible benefits of taking part?

The antioxidants present in the supplemented media have been thoroughly researched prior to their introduction in studies conducted outside of the UK. Similar studies have shown that embryos cultured in media containing these properties have comparable fertilization rates, embryo quality and improved ongoing pregnancy rates when compared to the standard media. In participants within the 35–40-year age group, supplemented media containing antioxidants have shown to improve embryo implantation rates when compared to the standard culture media. One study has also shown improved fertilisation rates for ICSI participants, with all other outcomes being similar between the antioxidant and standard media.

Your participation in the Gx Media Study may not directly benefit your treatment, however this research will help refine our processes within the laboratory and enable us to predict fertility treatment outcomes for future patients. This research will help us understand the influence of antioxidant media on embryo development within our own patient group.

What are the possible risks of taking part?

The risks involved in this study have been carefully assessed and the main objective of the research team is to ensure your gametes and embryos are treated with the same standard of care than they would receive if you were not a part of the study. HFC laboratory standard operating procedures and processes will be stringently adhered to when handling your gametes and embryos.
One possible risk associated with the Gx Media Study is slightly increased gamete and embryo handling within the laboratory, all other risks fall in line with those present during standard of care. There is currently no evidence or research which suggests the addition of antioxidants to culture media has a negative effect on treatment outcomes. As part of monitoring our key performance indicators, we consistently measure clinical outcomes to ensure our results are comparable to other clinics and European competency benchmarks. Should we see any indication that the use of antioxidant media is having a negative impact on clinical outcomes when compared to current success rates, the study will be ended prematurely.

Who is doing this research?

The Study is sponsored by Liverpool Women's NHS Foundation Trust, which holds appropriate indemnity and insurance cover, applicable to this study. The Gx Media study is being conducted by the Hewitt Fertility scientific team: Dr Rachel Gregoire is the study Principal Investigator, Bijal Patel (Chief Investigator), and Isheanesu Mutasa (Student Investigator).

Will my participation be confidential?

Yes, we will follow ethical and legal guidance and all information about your participation in study will be kept confidential. All data will be stored securely in accordance with the Data Protection Act 2018 and UK General Data Protection Regulation (GDPR).

Data collected by the research team from your clinical records will be recorded in a way in which you cannot be identified. The research team will assign you and your partner a unique study Identifier (ID) when you

consent to take part. This Study ID will be used to 'code' or pseudonymise data and remove any personal identifiable information.

A list of study IDs with associated personal identifiers will be maintained by the study team for the purposes of data linkage. This password protected document will act as a 'key' linking identifiable details such as your Name and Date of birth to the Study ID used to pseudonymise your research data.

Access to this password protected document will be controlled by the Chief Investigator, it will be stored on the Liverpool Women's NHS Foundation Trust secure, encrypted network and in a separate location to your research data.

To prevent unauthorised access to your personal details we will use things like encryption, password protected NHS computers systems, key card-controlled rooms and lockable storage cabinets to make sure your information is stored securely.

How will you use my data?

We will need to use information from your clinical records for this study. This information will Include your Name, Date of birth, Hospital Number and 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.

In order to protect your privacy, people who do not need to know who you are will not be able to see any of your identifiable information such as you name or contact details. Your data will have a unique study ID (or code), and this will be used to 'pseudonymise' the data.

We will keep all information about you safe and secure.

Once we have finished the study, we will keep some 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.

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.
- 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.

Where can you find out more about how your information is used?

You can find out more about how we use your information:

- at www.hra.nhs.uk/information-about-patients/
- our leaflet available from http://www.hra.nhs.uk/patientdataandresearch
- by asking one of the research team
- by sending an email to dataprotectionofficer@lwh.nhs.uk or
- by ringing us on 0151 702 4346.

What will happen to the results of the research study?

It is intended that once the study is completed and the results analysed, a summary of the results will be made available to you if you choose to receive them. If you would like to be informed of the findings from this research, there is an option on the consent form to opt in to receive them and provide the contact details you would like them to be sent to.

On completion of the study, the data will be analysed, tabulated and a final study report will be produced in the form of a master's level thesis of student investigator Isheanesu Mutasa.

If the results show that antioxidant media benefits our participants at HFC, we may introduce it as part of our standard operating procedures and make it available for all our participants, or those who would benefit most.

Who has reviewed the study?

This study has been reviewed and approved by the Health Research authority (HRA). All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee (REC). This study has been reviewed for ethical considerations and given favourable opinion by members of the North West - Preston Research Ethics Committee. The Human Fertilisation and Embryology Authority (HFEA) has confirmed the authorisation of this study under the existing HFEA treatment licence held by the Hewitt Fertility Centre, Liverpool.

Who should I contact for further information?

Should you have any further queries regarding this study, please contact:

Gx Media Study Team	
To speak with a member of the scientific team, arrange an appointment or for further information please contact: **Email:** isheanesu.mutasa@lwh.nhs.uk **Tel:** 0151 702 4241	For general enquiries please contact: LWFT Fertility Research team: **Email:** research@lwh.nhs.uk **Tel:** 0151 702 4346
Chief Investigator	**Principle Investigator**
Bijal Patel, Senior Clinical Embryologist, The Hewitt Fertility Centre, Liverpool Women's NHS Foundation Trust, Crown Street, Liverpool L8 7SS. Email: Bijal.patel@lwh.nhs.uk Tel: 0151 702 4121	**Dr Rachel Gregoire**, Scientific Director and HFEA person responsible, The Hewitt Fertility Centre, Liverpool Women's NHS Foundation Trust, Crown Street, Liverpool L8 7SS. Email: Rachel.gregoire@lwh.nhs.uk Tel: 0151 702 4173

Where can I get further information or discuss any problems?

If you have any questions or concerns about any aspect of this study, please contact a member of the research team, who will be happy to answer any questions or address any concerns you may have.

If you have raised concerns and feel these have not been resolved or for independent advice and support regarding your participation in the Gx Media Study, please contact:

Mr Andrew Drakeley,
Consultant Gynaecologist and Subspecialist in Reproductive Medicine, Honorary Associate Clinical Professor, University of Liverpool
Tel: 0151 708 9988
Email: Andrew.drakeley@lwh.nhs.uk

If you have a complaint, you feel you cannot come to us with or that has not been adequately addressed by the research team. Please contact Patient Advisory Liaison Service (PALS) on 0151 702 4353. You can also visit PALS by asking at the Liverpool Women's NHS Foundation Trust main reception.

Thank you for taking the time to read and consider this information sheet.