ARE YOU INTERESTED IN PARTICIPATING IN RESEARCH ON A NEW WAY OF SELECTING EMBRYOS?

During IVF, embryos are cultured in the laboratory for up to 5 days before embryo transfer by which time, embryos with a better prognosis have developed into blastocysts. On transfer day, an embryologist assesses their morphologic appearance and selects the one(s) with the highest chance of success for transfer.

Whether or not morphological assessment is the optimal method of embryo selection has been studied extensively over the past twenty years. Recently, a new decision support tool for embryo evaluation has been developed. Using deep learning, iDAScore® objectively "compares" a given embryo with others having similar development patterns and generates a score correlating with the likelihood of implantation.

The aim of this research is to investigate if embryo selection using the decision support tool iDAScore® can generate as many pregnancies as when the selection is performed by trained embryologists using conventional assessment only.

The research project is a multi-centre study conducted in clinics in Australia, Denmark, Hungary, Sweden, and the UK.

Eligible participants are patients undergoing IVF treatments at the recruiting clinics fulfilling the following:

- Embryo recipient up to 42 years
- Single embryo transfer performed on day 5
- Availability of at least two blastocysts on day 5

Participation does not involve any additional testing or extra visits to the clinic.

Hormone stimulation, oocyte pick-up and embryo transfer are performed according to the clinic's standard routines.

If you are interested in learning more or participating, please do not hesitate to contact us for further information.

Study Title: eValuating iDA Selection Ability. The VISA study
IRAS ID: 301947
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EVALUATING IDA SELECTION ABILITY. THE VISA STUDY.

WILL EMBRYO SELECTION THROUGH USE OF ARTIFICIAL INTELLIGENCE (IDA) PERFORM EQUALLY COMPARED TO DAY 5 MORPHOLOGY?

We invite you to take part in an international study called the VISA study. Before you decide it is important you understand why the research is being done and what it will involve. Please read the following information carefully. Please ask us if anything is unclear or if you would like more information. Take time to decide whether you wish to take part.

WHAT IS THE PURPOSE OF THE STUDY?

During IVF (in vitro fertilization), embryos are created in the laboratory and cultured for up to five days before embryo transfer by which time, embryos with a better prognosis have developed into blastocysts. On transfer day, an embryologist assesses their morphologic appearance and selects the one(s) with the highest likelihood of success for transfer.

However, morphological assessments have been shown to be inconsistent, subjective, and influenced by the experience level of the embryologist. Thus, many attempts have been made to find more objective methods for embryo selection. Recently, a new decision support tool for embryo assessment, based on artificial intelligence, called iDAScore® was developed. The iDAScore® is unique as it is completely based on machine learning, independent of any assumptions from previous knowledge of embryology standards and does not require any user input. It is intended to be used as an objective and reliable support tool in embryo evaluation.

The aim of the study is to investigate whether blastocyst selection supported by iDAScore® gives an equally high clinical pregnancy rate compared to when blastocyst selection for transfer is performed by trained embryologists using conventional morphology.

WHY HAVE I BEEN INVITED AND AM I ELIGIBLE?

Patients undergoing IVF treatment at the participating centres are approached. Patients undergoing freeze-all cycles can also participate. To be eligible you need to have a minimum of 2 early blastocysts on the day of embryo transfer. A total of 1040 patients will be enrolled at the participating IVF clinics in Australia, Denmark, Hungary, Sweden, and the UK. Study recruitment in the UK is planned between August 2021 and March 2022.

DO I HAVE TO TAKE PART?

No, it is completely up to you to decide. If you wish to participate you will be given this information sheet and asked to sign a consent form. After giving consent you can still withdraw at any time without giving a reason. Your decision to participate or withdraw does not affect the standard of care you receive.

WHAT DOES TAKING PART IN THE STUDY INVOLVE?

Participation does not involve any additional testing or extra visits to clinic. Procedures related to your treatment (hormone stimulation, oocyte pick-up and embryo transfer) are performed according to the clinic's standard routines.

Participants are randomly and equally divided between the two study groups. In the control group, the embryologist chooses the transferable embryo based on conventional morphology assessment only. In

the treatment group, embryo selection is performed by the embryologist, with additional support from iDAScore®. Surplus embryos are cryopreserved for later use in both groups.

The embryo transfer will proceed according to the clinic's standard operating procedures. Depending on the treatment outcome of your first embryo transfer within the current treatment cycle, your participation in the study lasts up to childbirth.

There is no greater access to IVF treatment through participation in the study.

CAN I KNOW MY RESULTS?

During your treatment, you will receive the same information regarding fertilization and embryo development on day 5 as non-participants. However, you and your clinician will be blinded to your group allocation and the scores of your embryos, if allocated to the iDAScore® group. The used selection technique can be shared with you after the embryo transfer.

WHAT IS THE PROCEDURE THAT IS BEING TESTED?

The iDAScore® algorithm is an automated computer analysis of developing embryos. Using deep learning, iDAScore® objectively "compares" a given embryo with others having similar development patterns, and generates a score correlating with the likelihood of implantation. This score can then be used to rank embryos and as such, as support in the important clinical decision of which embryo to primarily select for transfer. In the current study conventional embryo selection is compared to embryo selection supported by artificial intelligence.

ARE THERE ANY RISKS FOR ME IN JOINING THE STUDY?

If embryo selection supported by artificial intelligence is inferior to the conventional selection technique, subsequent embryo transfers may be required to achieve a pregnancy. This means that the time to pregnancy may be longer for the participants in the treatment group. However, the total chance of becoming pregnant during the IVF treatment is not negatively affected by participating as all surplus embryos of good quality are cryopreserved for later use.

In the treatment group, if the iDAScore® cannot be calculated due to unforeseen technical issues, study participation will end prematurely, and conventional morphology will be used to select the embryo to be transferred. If the embryologist is unsatisfied with the embryo selected by iDAScore, the embryologist may overrule this selection.

An independent data safety monitoring board has been appointed to follow the safety, efficacy, and the overall conduct of the study. The board consists of a statistician and a medically knowledgeable person, all unrelated to the study.

ARE THERE ANY BENEFITS FOR ME IN JOINING THE STUDY?

If embryo selection supported by deep learning is superior to the conventional selection technique, the time to pregnancy may be shorter in the treatment group.

Occasionally, some embryos in the treatment group may not fulfil the conventional criteria of cryopreservation but reach an acceptance level iDAScore®. These embryos will also be cryopreserved. This means that in some treatment cycles some extra embryos will be cryopreserved that otherwise would have been discarded. This will, if anything, increase the chance of a live birth as these embryos will be transferred later.

Your embryos will be cultured in an Embryoscope time-lapse system. This entails an undisturbed, stable culture environment with continuous monitoring of the development of your embryos. Your fresh transfer will be made in a transfer medium called EmbryoGlue®. This medium has been specifically developed to mimic the conditions of the female uterus to help embryos implant.

WHAT IF NEW INFORMATION BECOMES AVAILABLE?

Sometimes during a study, new information becomes available about the studied treatment. If this happens, your research doctor will contact you.

WHAT HAPPENS WHEN THE RESEARCH STUDY STOPS?

The iDAScore® is a commercially available, CE-marked medical device and its continued use in treatments is up to the clinics to decide.

WHAT IF SOMETHING GOES WRONG?

The risk of participants suffering harm because of taking part is minimal. Any adverse events related to study participation will be registered at the clinic and in the study database, analysed and processed. Any serious adverse events will also be reported to the relevant authorities.

Compensation for any injury caused by taking part in this study will be in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI). This applies in cases where it is likely that the injury results from a procedure carried out in accordance with the protocol for the study.

HOW WILL INFORMATION ABOUT ME BE KEPT CONFIDENTIAL?

This research will follow UK laws and regulations, such as the Data Protection Act, and the General Data Protection Regulation (GDPR). Several steps are taken to ensure confidentiality.

- Your consent to participate in the study will be recorded. The consent forms will be stored in a secure location at the clinic and separately from the study data.
- Study data is stored in a study database with restricted, password protected access. The study database is not connected to the database containing your medical records at the clinic.
- Your treatment number at the clinic will be crosslinked with a unique study identification number in the study database.
- Your medical records may need to be inspected by the company sponsoring the research for monitoring purposes. They may also be looked at by people from regulatory authorities to check that the study is being carried out correctly. Your name, however, will not be disclosed outside the clinic.
- For more details regarding data handling, we kindly refer you to the document “Vitrolife’s notice of personal data processing related to clinical trial participants”.

WHAT WILL BE STORED IN THE RESEARCH DATABASE?

Necessary study information will be collected by staff at the clinic from you and your medical records. The study database will not include any data that can identify you directly (surname, first name, address or similar). The database will include:

- Relevant background and health information, e.g., month and year of birth, details of your infertility history.
- Information about your current treatment, e.g., stimulation, embryo culture and outcome data.

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

The study is registered in a publicly accessibly database (clinicaltrials.gov, ID: NCT04969822). The results of the study will be published on the clinic's website and offered for publication in scientific journals regardless of the outcome. You will not be identifiable in any publication or report. We expect the results to be published within 12 months after the study has finished.

WHO IS ORGANIZING AND FUNDING THE RESEARCH?

The principal investigator of the study is A/Prof Peter Illingworth (Virtus Health/IVF Australia Western Sydney). The chief investigator in the UK is Professor Scott Nelson (see below for contact details).

The study is sponsored by Vitrolife, a global MedTech company. Vitrolife develops and manufactures a wide range of products and solutions for medically assisted reproduction, including culture media, disposables, and medical equipment.

WHO HAS REVIEWED/APPROVED THE STUDY?

The study procedures have been checked, reviewed, and agreed by the North West - Greater Manchester South Research Ethics Committee Research Ethics Committee.

WHO CAN I CONTACT IF I HAVE A QUESTION?

For more information, any concerns, or questions regarding the study, please feel free to turn to members of the clinic staff or any of the below contacts.

Clinic	Role/title and name	Contact details
TFP	Chief Investigator (UK), Scientific Director, Professor Scott Nelson	Scott.Nelson@glasgow.ac.uk Tel. 0141 201 8615
	Group Director of Embryology Lyndsey Zujovic	Lyndsey.Zujovic@tfp-fertility.com Tel. 0115 896 1900
TFP Nurture Fertility	Laboratory Manager Saran Ahitan	Saran.Ahitan@tfp-fertility.com Tel. 0115 896 1900
TFP Oxford Fertility	Laboratory Manager Anna Vincent	Anna.Vincent@tfp-fertility.com Tel. 01865 782 800
TFP Thames Valley Fertility	Laboratory Manager Danielle Breen	Danielle.Breen@tfp-fertility.com Tel. 01628 882 400
TFP Wessex Fertility	Laboratory Manager Tony Price	Anthony.Price@tfp-fertility.com Tel. 023 8070 6000

If you have any questions or queries regarding the processing of your personal data within the study, you are welcome to contact the Data Protection Officer at Vitrolife by sending an e-mail to dataprotection@vitrolife.com. If you are not happy with this response or believe your data is processed in a way that is not right or lawful, you can complain to the Information Commissioner's Office (ICO) (www.ico.org.uk or 0303 123 1113).

THANK YOU FOR YOUR INTEREST IN THIS STUDY!