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E-Freeze: Freezing of embryos in assisted conception

Submission date	Recruitment status	[X] Prospectively registered
24/12/2015	No longer recruiting	[X] Protocol
Registration date	**Overall study status**	[X] Statistical analysis plan
29/12/2015	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
29/07/2024	Pregnancy and Childbirth	

Plain English summary of protocol

Current plain English summary as of 07/05/2019:
Background and study aims
In order for a woman to become pregnant, the fertilised egg must attach (implant) itself to the lining of the womb. In vitro fertilisation (IVF) is a technique used to help people with fertility problems to have a baby. During IVF, couples donate their own sperm and eggs (or use sperm and eggs from a donor). The egg is fertilised by the sperm outside of the body to create an embryo and then returned to the woman's womb to develop, approximately three days later (fresh embryo transfer). Although IVF has become more and more successful in recent years, there is still a relatively high failure rate. In many cases, some of the embryos are frozen so that they can be thawed out and used in IVF at a later date (frozen embryo transfer). The aim of this study is to find out the effectiveness and cost-effectiveness of using frozen embryo transfer three months after egg donation, compared to fresh embryo transfer, and whether the technique used has an effect of the health of the baby at birth.

Who can participate?
Couples undergoing their first, second or third round of IVF fertility treatment at fertility centres in the UK.

What does the study involve?
Couples are randomly allocated to one of two groups. At the start of the study, all participants donate sperm and eggs so that embryos can be created. For participants in the first group, three days after egg donation, the fertilised embryos are placed in the female participants' womb. For participants in the second group, the fertilised embryos are frozen, for later use. These embryos are then thawed three months after the egg donation and implanted into the female participants' womb. Women in both groups are monitored to find out how many become pregnant. For those who do, the health of the baby is assessed by the medical team at the time of birth.

What are the possible benefits and risks of participating?
There are no immediate direct benefits of taking part in the study, but participating will help to inform future fertility treatment in the UK. There are no additional risks to the standard risks involved with IVF.

Where is the study run from?
Twelve fertility units in the Scotland and England (UK).

When is the study starting and how long is it expected to run for?
March 2015 to January 2021 (updated 08/07/2020, previously: June 2020)

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
1. Ms Christina Cole (public), christina.cole@npeu.ox.ac.uk
(updated 08/07/2020, previously: Ms Fiona Goodgame (public), fiona.goodgame@npeu.ox.ac.uk)
2. Dr Abha Maheshwari (scientific), a.maheshwari@abdn.ac.uk

Previous plain English summary:
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Study website
https://www.npeu.ox.ac.uk/e-freeze

Contact information

Type(s)
Public

Contact name
Ms Christina Cole

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University of Oxford
Old Road Campus
Oxford
United Kingdom
OX3 7LF
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christina.cole@npeu.ox.ac.uk

Type(s)
Scientific

Contact name
Dr Abha Maheshwari

Contact details
Aberdeen Maternity Hospital
Foresterhill
Aberdeen
United Kingdom
AB25 2ZL

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
N/A

Study information

Scientific Title
Freezing of embryos in assisted conception: a randomised controlled trial evaluating the clinical and cost-effectiveness of a policy of freezing embryos followed by thawed frozen embryo transfer, compared with a policy of fresh embryo transfer in women undergoing in-vitro fertilization.

Acronym
E-Freeze

Study objectives
The aim of this study is to determine if a policy of freezing embryos, followed by thawed frozen embryo transfer results in a higher healthy baby rate when compared with the current policy of transferring fresh embryos.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North of Scotland Research Ethics Committee, 12/11/2015, ref: 15/NS/0114

Study design
Pragmatic multi-centre parallel-group randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Other

Participant information sheet

Health condition(s) or problem(s) studied
Infertility

Interventions
Couples will be randomly allocated to either the standard care or intervention arm.

Standard care arm: Women will undergo fresh embryo transfer on day 3 or 5 (after egg collection).

Intervention arm: All good quality embryos will be frozen and couples will undergo frozen thawed embryo transfer within 3 months of the egg collection process. Couples will attend for a clinic visit and additional monitoring visits before frozen embryo transfer is performed.

Data be collected using bespoke electronic data collection forms at 6 time points between consent and 6 weeks post delivery. An emotions questionnaire will also be completed both after consent and at embryo transfer to understand how couples are feeling. And an economic questionnaire will be used to understand time and travel expenses accrued during their treatment.

Intervention Type
Procedure/Surgery

Primary outcome measure
Health of the baby is determined by medical staff at the time of birth.

Secondary outcome measures
1. Live birth rate
2. Pregnancy rate (defined as positive pregnancy test - 2 weeks after embryo transfer)
3. Clinical pregnancy rate (a pregnancy diagnosed by ultrasonic visualisation of one or more gestational sacs or definitive clinical signs of pregnancy; ectopic counts as clinical pregnancy; multiple gestational sacs count as one clinical pregnancy)
4. Ongoing pregnancy (pregnancy with presence of foetal heart beat)
5. Ovarian hyperstimulation syndrome (OHSS)
6. Miscarriage rate
7. Gestational diabetes mellitus (GDM)
8. Multiple pregnancy
9. Hypertensive disorders of pregnancy (comprising pregnancy induced hypertension; pre-eclampsia and eclampsia)
10. Antepartum haemorrhage
11. Preterm delivery (defined as delivery at <37 completed weeks)
12. Very preterm delivery (defined as delivery at <32 completed weeks)
13. Low birth weight (defined as weight < 2500 g at birth)
14. Very low birth weight (defined as < 1500 g at birth)
15. Large for gestational age (defined as birth weight >90th centile for gestation, based on standardised charts)
16. Small for gestational age (defined as less than 10th centile for gestational age at delivery)
17. Congenital anomaly (all congenital anomalies identified will be included)
18. Perinatal mortality (late as well as early neonatal deaths, up to 28 days after birth)
19. Evaluation of emotional state
20. Health economic outcome measures:
20.1. Costs to the health service of treatment, pregnancy and delivery care
20.2. Modelled long-term costs of health and social care, and broader societal costs

Overall study start date
01/03/2015

Completion date

31/01/2021

Eligibility

Key inclusion criteria
Current participant inclusion criteria (as of 24/01/2018):
1. The female partner is between 18 and 42 years of age at the start of treatment (i.e. start of ovarian stimulation)
2. Couples who are undergoing their first second or third cycle of IVF/ICSI treatment
3. Both partners are resident in the UK
4. Both partners are able to provide written informed consent

Previous participant inclusion criteria
1. The female partner is between 18 and 42 years of age at the start of treatment (i.e. start of ovarian stimulation)
2. Couples who are undergoing their first cycle of IVF/ICSI treatment
3. Both partners are resident in the UK
4. Both partners are able to provide written informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
1,086

Total final enrolment
619

Key exclusion criteria
Couples in whom:
1. Donor gametes are used
2. Pre-implantation genetic diagnosis is performed
3. Elective freezing of all embryos is preferred or clinically indicated (e.g. severe risk of OHSS)

Date of first enrolment
01/01/2016

Date of final enrolment
30/04/2019

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Aberdeen Maternity Hospital
Aberdeen Fertility Centre
Foresterhill
Aberdeen
United Kingdom
AB25 2ZL

Study participating centre
St Mary's Hospital
Department of Reproductive Medicine,
1st Floor
Oxford Road
Manchester
United Kingdom
M13 9WL

Study participating centre
Sheffield Teaching Hospitals
Jessop Wing, Assisted Conception Unit
Tree Root Walk
Sheffield
United Kingdom
S10 2SF

Study participating centre
King's College Hospital Assisted Conception Unit
Denmark Hill
London
United Kingdom
SE5 9RS

Study participating centre

Princess Anne Hospital
Complete Fertility Centre
Coxford Road
Southampton
United Kingdom
SO16 5YA

Study participating centre
Hewitt Fertility Centre
Crown Street
Liverpool
United Kingdom
L8 7SS

Study participating centre
Guy's and St Thomas' Assisted Conception Unit
11th Floor, Tower Wing
Great Maze Pond
London
United Kingdom
SE1 9RT

Study participating centre
Hammersmith Hospital
IVF Hammersmith
Du Cane Road
London
United Kingdom
W12 0HS

Study participating centre
Nurture Fertility
The East Midlands Fertility Centre
Interchange Business Park
Sandiacre
Nottingham
United Kingdom
NG10 5QE

Study participating centre

Homerton Fertility Centre
Homerton Row
London
United Kingdom
E9 6SR

Study participating centre
Oxford Fertility Unit
Nuffield Department of Obstetrics and Gynaecology
Oxford Business Park North
Oxford
United Kingdom
OX4 2HW

Study participating centre
Birmingham Women's Fertility Centre
Mindelsohn Way
Birmingham
United Kingdom
B15 2TG

Sponsor information

Organisation
NHS Grampian

Sponsor details
Research & Development
Foresterhill House Annexe
Foresterhill
Aberdeen
Scotland
United Kingdom
AB25 2ZB

Sponsor type
Hospital/treatment centre

Website
http://www.nhsgrampian.org/nhsgrampian/gra_display_home_2015.jsp?p_applic=CCC&p_service=Content.show&pContentID=9298&

ROR

https://ror.org/00ma0mg56

Organisation
University of Aberdeen

Sponsor details
Research Governance Office
Foresterhill House Annexe
Foresterhill
Aberdeen
Scotland
United Kingdom
AB25 2ZB

Sponsor type
University/education

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The research will be submitted for publication in high impact peer-reviewed scientific journals.

Intention to publish date
30/06/2021

Individual participant data (IPD) sharing plan
Applications for data sharing should be made to the NPEU CTU, using ctu@npeu.ox.ac.uk, with an accompanying protocol for the intended use of the data. This will be reviewed by the Trial Steering Committee or Data Controller if the TSC no longer exist. If approved, a Data Sharing Agreement will be compiled laying out the conditions to which the requestor must abide by. A cost may be incurred if the data requires additional work prior to sharing.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		13/06/2019	17/06/2019	Yes	No
Statistical Analysis Plan		30/06/2020	02/07/2020	No	No
Results article		06/01/2022	10/01/2022	Yes	No
Funder report results		01/05/2022	24/05/2022	No	No
HRA research summary			28/06/2023	No	No
Results article		13/06/2024	29/07/2024	Yes	No