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Reproductive function in teenage and young adult cancer survivors

Submission date 09/01/2023	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 03/03/2023	**Overall study status** Ongoing	[_] Statistical analysis plan [_] Results
Last Edited 08/05/2025	**Condition category** Cancer	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims
The treatment of cancer in young people is increasingly turning from focusing purely on survival to recognition of the long-term effects of treatment on subsequent quality of life. These issues are extremely important to patients and all involved in their care. In a recent UK research priority-setting initiative, research into the consequences of cancer was rated as a top priority by patients, their families, and healthcare professionals. That cancer treatment, including cytotoxic therapies, radiotherapy and surgery has adverse effects on fertility has long been recognised. In the ovary, chemotherapeutic agents affect growing follicles resulting in amenorrhea and in the longer-term loss of fertility and premature ovarian insufficiency (POI). For males, sperm counts can be very low after treatment, but in some there can be full or partial recovery.

Who can participate?
Any patient aged 13-25 years old with a new cancer diagnosis or presenting with a recurrence of cancer that requires treatment

What does the study involve?
A single blood sample and data collection are conducted at baseline, and 1-, 2-, 3- and 5-year follow-up. Where possible, the study visits will coincide with a clinical visit.

What are the possible benefits and risks of participating?
Patients will not benefit from participating in the study. As this is an observational study, no adverse events are expected. There is a risk of minor bruising after a blood sample is taken.

Where is the study run from?
University of Edinburgh (UK)

When is the study starting and how long is it expected to run for?
January 2021 to January 2027

Who is funding the study?
Medical Research Council (UK)

Who is the main contact?
Audrey Kuchnowski audrey.kuchnowski@ed.ac.uk (UK)

Contact information

Type(s)
Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
285290

Protocol serial number
CPMS 49696, IRAS 285290

Study information

Scientific Title
Reproductive function in teenage and young adult cancer patients in the UK

Acronym
The PROTECT study

Study objectives
This study will undertake an analysis of the effects of cancer treatments on reproductive function in teenagers and young adults (TYA) to address the hypothesis that cancer diagnosis, cancer treatment and age at treatment affect fertility-related biomarkers and hence long-term fertility/reproductive health in survivors. This is a multi-centre clinical prospective observational cohort study open to clinical centres directly involved in the care of TYA (aged 13-25) with cancer. Previous studies are retrospective thus assessing historical treatments, and mostly rely on questionnaire-based self-reported outcomes, introducing the opportunity for bias and inaccuracy. Additionally, there is a need for data specific to this post-pubertal age group, distinct from children.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/07/2021, South West - Frenchay Research Ethics Committee (Ground Floor, Temple Quay House, 2 The Square Bristol, BS1 6PN, UK; +44 (0)207 104 837; frenchay.rec@hra.nhs.uk), ref: 21/SW/0039

Study design
Prospective observational cohort study

Primary study design
Observational

Study type(s)
Prevention

Health condition(s) or problem(s) studied
Cancer and reproductive health

Interventions
This is a multi-centre clinical prospective observational cohort study open to all clinical centres directly involved in the care of teenage and young adults (aged 13-25 years) with cancer.

Potentially eligible patients will be identified by the research team and/or clinical team looking after them. After an initial assessment, potentially eligible patients will be assessed for study inclusion by the assessing clinician and/or member of the research team. If the patient fulfils the study eligibility criteria and is deemed to be competent and have the capacity to consent, an

appropriately delegated member of the study team will take written informed consent. It will be documented in the patient's medical notes that they were deemed eligible and capable of providing written informed consent. There will be the option for parents/guardians to provide consent on behalf of those patients who are eligible and willing to take part in the study but are not capable of providing written informed consent.

The study aims to recruit 1000 participants over a period of 5 years, approx. equally males and females.

Participants' demographics, clinical data including PMH, diagnosis information, treatment information and biological samples will be collected locally at study sites at the following timepoints: baseline, one year after diagnosis and annually thereafter for five years (in the first instance with the intention to extend follow-up). An additional blood sample will be obtained as part of the study to measure anti-Mullerian hormone (AMH) in serum (in females) and Inhibin B in serum (in males). These samples will be transported to the lead site (Edinburgh) for storage and analysis.

This study is proposed in collaboration with the Teenage and Young Adult CSG of the National Cancer Research Institute (NCRI). The NCRI is a UK-wide partnership which promotes collaboration in cancer research. Study documentation will be reviewed by the Teenage and Young Adult group of the National Cancer Research Institute (NCRI).

Intervention Type
Other

Primary outcome(s)
Prevalence of reproductive failure and of gonadal dysfunction measured using diagnosis /treatment regimen at 2 years after diagnosis

Key secondary outcome(s))
Current secondary outcome measures as of 08/05/2025:

Uptake of fertility preservation services, and long-term reproductive outcomes including ongoing ovulation/spermatogenesis, conception, age at menopause, and the need for hormone replacement. The prevalence of reproductive failure and of gonadal dysfunction by diagnosis /treatment regimen at 1 and 5 years after diagnosis. A blood sample is collected at baseline, and 1-, 2-, 3- and 5-year follow-up. In females, anti-Mullerian hormone (AMH) levels will be measured in serum, data will be analysed in conjunction with follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E2) levels. For males, Inhibin B will be measured in serum. Inhibin B data will be analysed in conjunction with FSH/LH/testosterone levels.

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Previous secondary outcome measures:

Uptake of fertility preservation services, and long-term reproductive outcomes including ongoing ovulation/spermatogenesis, conception, age at menopause, and the need for hormone replacement. The prevalence of reproductive failure and of gonadal dysfunction by diagnosis /treatment regimen at 1 and 3 years after diagnosis. A blood sample is collected at baseline, and 1-, 2- and 3-year follow-up. In females, anti-Mullerian hormone (AMH) levels will be measured in

serum, data will be analysed in conjunction with follicle-stimulating hormone (FSH), luteinizing hormone (LH) and estradiol (E2) levels. For males, Inhibin B will be measured in serum. Inhibin B data will be analysed in conjunction with FSH/LH/testosterone levels.

Completion date
31/03/2030

Eligibility

Key inclusion criteria
Current inclusion criteria as of 28/01/2025:
1. Willing and able to provide written informed consent (including by parent/guardian where appropriate)
2. Aged 13-25 years
3. First cancer diagnosis or relapse of same diagnosis
4. Requires cancer treatment with targeted, immunological and cell-based therapies (surgery, chemotherapy and radiotherapy are permitted if part of this treatment or if the initial treatment plan changes)

Previous inclusion criteria:
1. Willing and able to provide written informed consent (including by parent/guardian where appropriate).
2. Aged 13-25 years old
3. First cancer diagnosis
4. Requires cancer treatment (surgery, chemotherapy including targeted therapies, radiotherapy, bone marrow transplant).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
13 years

Upper age limit
25 years

Sex
All

Total final enrolment
532

Key exclusion criteria

1. Inability to provide informed consent
2. Does not require cancer treatment
3. Where treatment is not given with the intention of cure or long-term survival

Date of first enrolment
28/01/2022

Date of final enrolment
30/12/2024

Locations

Countries of recruitment
United Kingdom

England

Scotland

Wales

Study participating centre
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
St James's University Hospital
Beckett Street
Leeds
United Kingdom
LS9 7TF

Study participating centre
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre
Gartnavel Royal Hospital
1055 Great Western Road
Glasgow
United Kingdom
G12 0XH

Study participating centre
Queens Medical Centre
Derby Road
Nottingham
United Kingdom
NG7 2UH

Study participating centre
University College London Hospital
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
United Kingdom
B15 2GW

Study participating centre
Royal Sussex County Hospital
Eastern Road

Brighton
United Kingdom
BN2 5BE

Study participating centre
University Hospitals Bristol and Weston NHS Foundation Trust
Trust Headquarters
Marlborough Street
Bristol
United Kingdom
BS1 3NU

Study participating centre
Cardiff & Vale University Lhb
Woodland House
Maes-y-coed Road
Cardiff
United Kingdom
CF14 4HH

Study participating centre
Royal Devon and Exeter Hospital
Barrack Road
Exeter
United Kingdom
EX2 5DW

Study participating centre
Royal Marsden Hospital
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
Sheffield Children's Hospital
Western Bank
Sheffield
United Kingdom
S10 2TH

Study participating centre
Northern General Hospital
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
James Cook University Hospital
Marton Road
Middlesbrough
United Kingdom
TS4 3BW

Study participating centre
Southampton General Hospital
Tremona Road
Southampton
United Kingdom
SO16 6YD

Study participating centre
Bristol Haematology & Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Study participating centre
Bristol Royal Hospital for Children
Paul O'Gorman Building
St Michaels Hill
Bristol
United Kingdom
BS2 8BJ

Study participating centre
Castle Hill Hospital
Castle Road

Cottingham
United Kingdom
HU16 5JQ

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
Derriford Hospital
Derriford Road
Plymouth
United Kingdom
PL6 8DH

Study participating centre
Freeman Road Hospital
Freeman Road
High Heaton
Newcastle upon Tyne
United Kingdom
NE7 7DN

Study participating centre
Great North Children's Hospital, (Royal Victoria Infirmary)
Victoria Wing
Newcastle upon Tyne
United Kingdom
NE1 4LP

Study participating centre
Leeds Children's Hospital
Leeds General Infirmary
Clarendon Wing
Great George Street

Leeds
United Kingdom
LS1 3EX

Study participating centre
Nottingham University Hospitals - City Campus
Nottingham City Hospital
Hucknall Road
Nottingham
United Kingdom
NG5 1PB

Study participating centre
Royal Hospital for Children and Young People
50 Little France Crescent
Edinburgh
Lothian
United Kingdom
EH16 4TJ

Study participating centre
St. Bartholomews Hospital
West Smithfield
London
United Kingdom
EC1A 7BE

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
Glasgow
United Kingdom
G12 0YN

Study participating centre
Christie Hospital
Wilmslow Road
Manchester
United Kingdom
M20 4BX

Study participating centre
University Hospital of Wales
Heath Park
Cardiff
United Kingdom
CF14 4XW

Study participating centre
Weston Park Hospital
The University of Sheffield
Whitham Rd
Broomhall
Sheffield
United Kingdom
S10 2SJ

Sponsor information

Organisation
University of Edinburgh and NHS Lothian

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Professor Anderson, including anonymised IPD, from credentialed academic researchers

IPD sharing plan summary
Available on request