NCRI Teenage and Young Adult and Germ Cell Tumour (TYA & GCT) Group

Annual Report 2020 - 2021

NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of the NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.

List of Appendices

NCRI TYA & GCT Group

Annual Report 2020-21

1. Top achievements in the reporting year (up to three)

Achievement 1

We have influenced NHS practice in 2 strategic target areas:

(i) The TYA Cancer Survivorship Study arose from this Research Group. The cohort of over 200,000 young people linked through registry databases has identified significant adverse health risks. Survivorship Subgroup members are part of the latest publication international clinical follow-up guidelines for TYA. The results of this have informed the latest NHS service specification in this year. Each TYA cancer survivor is stratified as low, medium or high risk based on the results of our study.
(ii) The TE24 (TRISST) study, developed in the Germ Cell Group, was disseminated in 2020 to address a key strategic issue in germ cell NHS practice. This informs national policy on the management of the germ cell tumour seminoma for the majority of patients, reducing radiation exposure (therefore late effects) and saving NHS resource (fewer scans).

Achievement 2

Achieved each of the 3 priorities of the main Research Group from 2019-2020.

(i) We have a TYA-specific working project agreed with the Experimental Cancer Medicine Centres infrastructure, including both the Experimental Cancer Centres but also other NHS settings where TYA receive care. This can underpin increasing in tumour and host biology research in TYA also (q.v. our 2021 quinquennial review).
(ii) We have a reproductive function study approved, building from industry pump-priming to national collaboration.
(iii) We have recruited a substantial expansion in our PPIE enabling a wider range of people living with TYA cancer and/or GCT to contribute to our work.

Moreover, we have joined these objectives up, strategically – The wider PPIE group recently contributed to the reproductive function grant application, which includes the effects of experimental cancer medicines upon TYA fertility.

Achievement 3

BRIGHTLIGHT and BRIGHTLIGHT_2021

We have published both the primary and secondary outcomes for the BRIGHTLIGHT study, and several papers from workstream 1 and our PPI. We successfully secured, through a two-stage competitive funding call, funding for the BRIGHTLIGHT_2021 study. Although, not a substantial amount of funding, the work is critical to confirm or refute a specific outcome of the original 2011-2019 BRIGHTLIGHT NIHR applied programme grant developed by this Research Group. This was the key observation that for patients receiving care during 2012-14 which was delivered between a Principal Treatment Centre and a Designated Hospital, this care was associated with poorer outcomes and higher NHS and patient costs. However, since recruitment to BRIGHTLIGHT in 2012-14, the NHS has evolved this relationship between Principal Treatment Centres and Designated hospitals. A key finding of workstream 1 was that

the culture of TYA care, the maturity of the multidisciplinary team and the links with networked hospitals all took time to develop. Therefore, to inform NHS policy, of 'enhanced joint care' this key observation from 2012-14 requires replication. We are involving the devolved nations in BRIGHTLIGHT_2021 with supplementary funding from UCLH.

2. Structure of the Group

Looking forward to 2021-22, the NCRI TYA & GCT Group now faces some instability as the dedicated research support for the Group will cease at the end of this reporting year. Key work in PPIE, Health Services Research, studies of recruitment to clinical trials and of pathways to diagnosis will be in transition. That several of these have been so successful (q.v. our 2021 Quinquennial Review [QQR]) is a clear credit to Lorna Fern, but also to the power of the specific dedicated research support that has been in place until now. We have a transitional plan, but there are risks in this.

No other structural changes have taken place this period. We have had a moratorium on membership changes other than substantially increasing our PPIE members. We are soon seeking new trainee members, as those came to a successful end to their terms. We will seek new members this year following our strategy meeting.

We welcome recent new members from before the moratorium: Paul Chumas (Neurosurgery); Ben Fulton (Clinical Oncology); Constantine Alifrangis (Medical Oncology).

We welcome new service user members: Emma Williams, Kyle Blain, Bethany Mickleburgh, Charlotte Wickens, Pippa Simpson and Josh Henderson. They are joining the Subgroups of our Research Group and will contribute to the main Group on rotation.

Hadeel Hassan has come to the end of her term as trainee member. She has been very successful in building the digests of the NCRI Group work, that she is finalising disseminating before undertaking a clinical training fellowship in Canada. We are aiming to appoint new trainee members very soon.

The Chair and other members have built further specific *international* multidisciplinary research links this period, including with the European Society for Medical Oncology (ESMO), the European Society for Medical Oncology (SIOPE), the European Oncology Nursing Society (EONS) and the European School of Haematology (ESH) around TYA cancer research. This is strategic, given the strong possibility of funding for TYA programmatic research within Horizon Europe, to examine our patterns of research funding, looking at CRUK and other sources, and carry out any shifts that may be necessary (q.v. 2021 QQR).

3. TYA & GCT Group & Subgroup strategies

The Teenage and Young Adult and Germ Cell Tumours (TYA & GCT) Research Group as a whole (Main Group and Subgroups) contributes with its' specific research to the overall purpose of the NCRI;

- Ensure a coordinated portfolio of research related to cancer
- Seize opportunities and address challenges in research relevant to cancer
- Improve the quality and relevance of research related to cancer
- Accelerate translation of cancer-related research into practice

The Research Group will work collaboratively within and between our various Subgroups under several research themes:

- Trials
- Germ Cell Tumours
- Survivorship
- Biology
- Healthcare provision
- Joint working
- Impact

TYA & GCT main Group.

This Group aims to be the home of studies that are wider or larger than the Subgroups, requiring further collaboration or inter-subgroup co-operation.

The specific objectives of the main Group which were achieved for the 12-month period to March 2021 were:

i. A national prospective reproductive function study, in young adult cancer patients across the UK.
ii. Understanding TYA radiotherapy outcomes - develop a biological study after 2019 workshop.
iii. Developing further research into the clinical pharmacology of TYA with cancer, with the Experimental Cancer Medicine Centres.

We had 2 ongoing objectives from 2018-20 that were incomplete:

iv. Assess, influence and re-assess our impact as a Group upon our clinical and research community. Collaborations with other site-specific groups and dissemination.
v. Trial participation in TYA as an applied health research project, another unsuccessful bid to the NIHR was submitted. Disappointingly, it was deemed 'out of remit' again, despite working with the NIHR Research Design Service extensively prior to submission.

We report considerable progress against these:

i. Reproductive function: We have achieved approval for our TYA-specific study in fertility. This strengthens our industry relationship as requested in our 2018-19 feedback letter. Every TYA PTC and 3 TYA designated hospitals have expressed a wish to recruit to the study. An MRC supporting science grant is submitted May 2021. NIHR portfolio adoption and multi-centre ethical approval have been sought.
ii. TYA radiotherapy outcomes: This has developed in outline, but the lead clinical oncologist has been unable to maintain capacity to do this work, and not been able to be replaced despite requests to CTRad. Other approaches are being made.
iii. To build a working relationship for TYA with the Experimental Cancer Medicine Centres (ECMC) research infrastructure: This can ensure TYA issues with trial enrolment are addressed from the beginning of the history of a cancer treatment. This will be highly

collaborative, with ACCELERATE and the ECMCs for children and adults, and provide improvements in clinical trial entry beyond our specific demographic. This can strengthen our industry relationships as requested in previous feedback letters.

iv. Site-specific groups:
    a. We have met with the Children's Group Leukaemia Subgroup and have a policy in place to share studies early in their development.
    b. We have disseminated several precis of our working meetings to our wider community. We will repeat our 2019 community survey to understand our impact and wider opportunities for engagement.
v. A cohort evaluation of new NIHR trial participation investment: The NIHR was unable to make the investment in improving the TYA research infrastructure that this study was to be based upon. This NHS/NIHR change is now developing sadly only piecemeal and variably geographically. Therefore, we will return to this study when it is timely.

Our delivery against these objectives is best seen in context of our overall strategic aims as a cross-cutting TYA & GCT main Research Group 2018-21: Our overall progress against our 2018-21 objectives are below, indicating our timely progress:

Project	Lead individual	Others involved	Type	Milestone	Milestone Date	Output	Output date	Progress at May 2021
Form a Germ Cell Subgroup	Jonathon Shamash	None	New	Application submitted	Sep-18	Subgroup met	Mar-19	Completed New Chair appointed: Alison Reid
Evolve the main Group meeting	Dan Stark	None	New	New agenda agreed and used	Dec-18	New Agenda evaluated	Dec-19	Completed New format standard for meetings is in place
Identify TYA leads for key site-specific Research Groups.	Dan Stark	NIHR	Continuing	First Research Group TYA lead named	Oct-18	1st study submitted with James Lind Alliance (JLA) issue as sub-study	Jun-21	Completed See 2019-20 annual report
Answer a JLA TYA question in a site specific clinical trial	TBC	Other site-specific Research Groups.	New	Engagement with a site-specific Research Group TYA lead	Oct-18	Open a study addressing a JLA TYA question	May-21	Ongoing engagement with the leukaemia group
Influence the NHS processes that deliver trial recruitment	Lorna Fern	NHS England Clinical Reference Groups (NHSE CRG)	Continuing	None	None	Comment on NHSE Service Specification.	Dec-18	Completed Meetings with NCRI Group Chair, NHSE CRG Chair and TCT Director of Research are now completed
Digital interventions, artificial intelligence and machine learning	Dan Stark	Health Services Research Subgroup, Biological	New	Agree digital platform with a commercial or academic partner	Mar-19	Workshop on digital data and artificial intelligence	Nov-19	Application made to the NCRI Horizon Call but unsuccessful

		Studies Subgroup						Masters project in School of Computing in 'Artificial intelligence to improve informed consent for clinical trials in TYA' scheduled to commence September 2021 (Leeds)
Consumer involvement improved	Lorna Fern	Germ cell charities, Germ Cell Tumour S ubgroup, Health Services Research Subgroup	Continuing	Meeting with Germ cell nursing	Sep-18	Test new model on germ cell MiRNA study	Mar-19	Completed Results published.
Available recruitment data for TYA into trials	Dan Stark	NIHR	Continuing	Edge database amended	Nov-18	Trial data presented to main Research Group	Dec-19	Completed with the NIHR CTYA Lead. Completed year of age to be included as a core data point for all individuals entering NIHR portfolio trials
Study of fertility after Adolescents and Young Adults (AYA) cancer	TBC	Germ Cell Tumour Subgroup, Biological Studies Subgroup, Health Services Research Subgroup	New	Study design group formed	Dec-19	Study design with pilot data presented to Research Group	May-21	Completed Study in set up.
Messaging enhanced from Research Group	Dan Stark	None	New	None	None	Messaging sent second time	May-19	Partially Completed Meeting digests distributed via charities. Second survey to follow

Data about impact of the TYA & GCT Research Group	Martin McCabe	NCRAS	New	Identify existing NCRAS and patient survey data which addresses research	Dec-20	Further surveys of impact of Group designed studies	Jun-21	Ongoing Difficult to extract data due to lack of resource in NCRAS

New projects have begun in this reporting period also:

i. To innovate in PPIE, allowing a wider range of TYA to contribute without needing time away from work and education. We have recruited 5 further consumer members and worked with them in consultation on several projects including feedback upon CRUK grants and our fertility study. The challenge is delivering this work sustainably, with the changes in group support.
ii. We have secured a masters project in the School of Computing (Leeds) in 'Artificial intelligence to improve informed consent for clinical trials in TYA' scheduled to commence September 2021.
iii. CRUK Grand Challenge application in Sarcoma – we are a collaborating group on the outline submitted by Burchill et al. in 2021.

The single largest challenge to our identifying our success around improving recruitment of TYA to cancer research is the lack of data on the age of patients entering NIHR portfolio clinical trials. This should feature strongly in our 2021-24 strategy, we expect.

Germ Cell Tumour Subgroup (Chair, Dr Alison Reid)

The overall aims of the Germ Cell Subgroup are:

- To improve clinical outcomes for patients with germ cell tumours by conducting high quality research that changes NHS practice.
- To widen the breadth and impact of GCT research expertise through academic collaboration

The specific objectives of this group for this 12-month period to March 2021 were:

i. Implementation of circulating microRNA assay into germ cell tumour management
ii. Patient and Public Engagement Improved
iii. Age and GCT outcomes
iv. Stratified treatment in resistant disease
v. Studies to reduce toxicity and maintain efficacy

We have:

i. Implementation of circulating microRNA assay into germ cell tumour management: Published on methods (for clinical implementation), and clinical relevance as well as novel PPIE methods, and embedded sample collection in a host of global clinical trials and other protocols.
ii. Patient and Public Engagement Improved: In addition to an existing PPIE representative who is a germ cell tumour survivor, we have recruited a further male and a female germ cell tumour survivor to our PPIE panel. This has happened alongside the publication in this reporting period of our novel PPIE approach in GCT, where we embedded qualitative examination of a series of PPIE events in a set of patient support groups to evaluate the impact of MiRNA to replace CT scan in GCT surveillance.
iii. Age and GCT outcomes: Subgroup members provided data and leadership (Shamash, Huddart, Stark) in the latest work of the International Germ-Cell Cancer Collaborative Group (IGCCCG) in this reporting period. This updates on and develops the seminal work of the 1990s on risk classifying germ cell tumours. Age as a risk factor is introduced for the first time.
    a. DOI: 10.1200/JCO.20.03292. Journal of Clinical Oncology 39 published online March 17, 2021.
    b. DOI: 10.1200/JCO.20.03296 Journal of Clinical Oncology 39, Published online April 06, 2021.

    This is leading to a planned overarching epidemiological study in GCT (see Quality of Life & Survivorship Subgroup bullet ii).

iv. Stratified treatment in resistant disease: A specific experimental cancer medicine proposal to Cancer Research UK by the Oxford group was unsuccessful previously. This can now be developed further within the TYA experimental cancer medicine initiative (see main Group)
v. Studies to reduce toxicity and maintain efficacy: The Subgroup Chair is initiating a project to examine the patterns of treatment delivered to patients with advanced germ cell tumours aged over 40, amalgamating routine clinical data (NCRAS, SACT, NHS footprint for late effects, existing biological data (GCIP), and clinical report of treatment approaches). This might lead to an intervention study in older GCT patients in our next strategic review.

These achievements are best seen in context. Our Subgroup objectives 2018-21 have been:

- Lead new studies, with UK study design and leadership and UK funding sought, reducing toxicity in good prognosis disease and increasing efficacy in poor prognosis disease
- Deliver timely UK-wide participation in existing studies.
- Collaborate with other main Research Groups, Subgroups and elsewhere to develop our research, in areas such as late effects, survivorship care, patient and public involvement, age-treatment interactions and the impact of our research.
- Integrate female germ cell tumour research with the stronger previous research in male germ cell tumours.
- Work with international collaborators in the globalised germ cell research world, including the G3, MAGIC and other global groups.
- Strengthen the relationship between the paediatric and adult-trained clinical researchers in germ cell tumours in studies of patients aged >11 years.

We have made fair progress against these objectives in 2020-21. The specific timed aims are listed below. The recruitment of expertise in female germ cell tumours commenced at the February 2021 Subgroup meeting, with names identified and approaches ongoing. Timely participation in trials has recommenced after 12 months of limited feasibility. The relationship between paediatric and adult-trained individuals is entirely embedded now. The international working is entirely embedded now. The UK leadership in trials is apparent in AGCT1531, P3BEP, Micro-RNA development and testing, PROs and consumer engagement.

Project	Lead individual	Others involved	Type	Milestone	Milestone Date	Output	Output date	Progress
Studies to reduce toxicity and maintain efficacy	Jonathon Shamash	None	Continuing	Studies discussed in the new group	Jun-19	Submission for funding	Mar-20	AGCT 1531. Carboplatin in seminoma trial successful via MAGIC collaboration
Stratified treatment in resistant disease	Andrew Protheroe	MAGIC	New	None	none	Funding application	Dec-19	Unsuccessful grant CRUK 2020
CXC-12 study	Robert Huddart	None	Continuing	None	none	Funding application	Dec-18	Progressing within AGCT 1531 and P3BEP
The implementation of micro-RNA in germ cell tumour management	Matt Murray	MAGIC, G3	Continuing	None	none	Proposal for NHS implementation	May-20	Progressing within AGCT 1531, P3BEP, TIGER and other fundamental science and clinical research. Embedded in trials, in the US SWOG (Craig Nicholls) using serum microRNA371a-3p to inform clinical decisions on RPLND - 90-95% sensitivity. Better than PET
Age and GCT treatment and outcomes	Richard Feltbower	NCRAS	New	Methodologist (registry) agreed	May-19	Analysis of age and management outcomes in GCT	May-21	AYA outcomes published. Collaboration proposed for older non-seminomas at testis Subgroup and main Group 2020-21

New projects have begun in this reporting period also:

Several proposals for the next generation of international seminoma MAMS trials of surgical and non-surgical approaches are being led within by Subgroup and the Group within the MAGIC and G4 groups.

The Subgroup is actively working on two clinical trial proposals that address treatment de-escalation while aiming to maintain efficacy. These include THERATEST – THERapy de-escalation for TESTicular cancer patients and OTIS- Optimising Therapy In Seminoma patients.

THERATEST: This study is proposed as a Phase II cohort-embedded trial of primary robotic retroperitoneal lymph node dissection (rRPLND) for IGCCCG "good risk" metastatic testicular cancer. The group is working with Mr Rajan, urological surgeon, on the trial design and funding has been secured from the Barts Charity for the 30-patient Phase II. If the primary endpoint of feasibility of recruitment/ retention is met in this study, this would serve as a platform for a larger study addressing outcomes and patient experience.

OTIS: This is a proposed multi-centre trial for good prognosis metastatic seminoma patients aiming to potentially de-escalate treatment for selected patients. In addition to being discussed at national level, the trial is being discussed at the international MAGIC consortium. The trial proposes to incorporate miRNA studies to stratify patients and possibly FDG-PET imaging in the design. Endpoints include disease free survival >90% for each experimental strategy, quality of life and health economic measures.

Our 2021 QQR report serves to emphasise the priority that should be given to this Subgroup's work in the next 3 years strategy review. They comment:

- The Group demonstrated a strong legacy of research in GCT, that has been practice-changing, such as the 111 study.
- The Group would benefit from representation in the following expertise: female germ cell tumours, gynaecological oncology, urology, endocrinology, surgeons, population science and behavioural science
- Whether GCTs were receiving the focus that they require and questioned whether GCT being a Subgroup is the best approach
- This area of research is an opportunity to attract young investigators to run international trials. We are awaiting the development of this scheme within NCRI, and have candidates waiting.

Quality of Life and Survivorship Subgroup (Chair, Professor Mike Hawkins)

This group aims to:

- identify and characterise substantially elevated adverse health outcomes in TYA living after cancer.
- determine opportunities for prevention and other interventions aimed at risk reduction.
- extend the available research data about TYA living after cancer.
- study models of NHS care for TYA living after cancer.

The specific objectives of this Subgroup for this 12-month period to March 2021 were:

i. New TYA Cancer Survivor Studies (TYACSS) linkages.
ii. Plan germ cell LE analyses.
iii. Develop new models of follow up evaluation or trial.
iv. Cerebrovascular Case-control study.
v. Impact of research.

Progress upon each of these has been considerable:

i. **TYACSS linkages:** Later in 2021 we plan to produce a publication relating to the entire TYACSS cohort of 200,000 5-year survivors which will be based on the linkages across all national morbidity/mortality databases available (specifically the Hospital Episode Statistics, cancer registration and death registration databases) to investigate a total burden of disease experienced by survivors and use this to:
   - Provide risk stratification information for survivors which identifies subgroups of survivors who experience low/medium/high risk of serious adverse health outcomes.
   - Such risk stratification will be useful in preparing individual care plans for survivors and in providing evidence to update both NHS-E Service Specifications and clinical follow-up guidelines.

   In progress are electronic linkages to recently available national databases to gain further insight into the spectrum of consequences experienced by cancer survivors including linkages with:
   - the national NHS GP prescription database available via PHE.
   - the Mental Health Services Database maintained by NHS Digital.

   One PhD student funded by a studentship awarded by PHE is investigating the risks of GP prescriptions indicative of mental health conditions among the 200,000 5-year survivors in the UK Teenage and Young Adult Cancer Survivor Study (TYACSS). Another PhD student is investigating adverse conditions in pregnancy, pregnancy outcomes and livebirth rates among female survivors included in the TYACSS cohort using information available from linkage with the national HES database.

ii. **Plan germ cell LE analyses:** Although no investigations relating exclusively to germ cell tumours have been undertaken, all outputs reported under: "(i) TYACSS linkages" are of considerable interest in relation to survivors of any specific type of cancer including germ cell tumours. For example, in the population-based national UK TYACSS cohort there are 24,309 and 4885 5-year survivors of testicular and ovarian cancer, respectively, and so the risk stratification evidence provided in relation to germ cell tumours is likely to be unprecedentedly informative, unbiased (because of the population-based design) and reliable (because of the numbers available).

iii. **Develop new models of follow up evaluation or trial:** After initial disinterest from the clinical community outside of 2 leading centres (Leeds and Southampton), more recently changes in services due to COVID-19 have resulted in considerable interest in this reporting period. A multicentre Nursing PhD proposal is in preparation 2021-22 (Led Stark Leeds/Wheater Southampton) as a collaboration with the Germ Cell Tumour Subgroup. This plans to develop an industry (information technology), service user and service provider collaboration, develop a unified multicentre model of community-based clinical follow-up after germ cell tumour, and pilot that model in an NIHR PhD fellowship for Saalmink, a talented academic nurse.

iv. **Cerebrovascular Case-control study:** We have established a national Advisory Group to develop an investigation aimed at intervening to reduce the substantially increased risk of hospitalisation for stroke among TYA cancer survivors, particularly after irradiation for CNS tumour, head and neck cancer and leukaemia. The foreseen components include:
   - Using MRI (with MRA) imaging to investigate the developmental mechanisms leading to stroke, particularly in relation to time from radiation exposure, with a view to identifying opportunities for preventative interventions.
   - Explore potential preventative interventions including avoidance of under diagnosis/under treatment for hypertension, dyslipidaemia and diabetes with appropriate pharmacological interventions. Also explore potential lifestyle interventions.

- Undertake a case-control study to understand aetiological factors including radiation dose from radiotherapy, cumulative dose of specific cytotoxic drugs, lifestyle factors from a questionnaire including smoking and saliva for genotypic factors.
- Use the case-control study measures of excess risk, together with general population risk estimates, to develop individual risk prediction models for these events in the survivor population.
- Such risk prediction models and the imaging studies would be useful in evaluating the potential utility of screening/surveillance to identify developing abnormalities at an early stage.
- Develop evidence-based clinical follow-up guidelines for clinicians following-up these survivors.

An application to the NIHR Programme Grant for Applied Research funding stream is anticipated.

v. **Impact of research:** Evidence produced in our risk stratification publication published in the "British Journal of Cancer" was used by NHS England in its latest Service Specification, which is in implementation in the current reporting period. Specifically, the clinical follow-up of every TYA cancer survivor in England should be assessed using our risk stratification tool to determine whether the risks of long-term serious adverse health outcomes is low, medium or high: https://www.engage.england.nhs.uk/consultation/teenager-and-young-adults-cancer-services/user_uploads/service-specification-tya-principal-treatment-centres-and-networks.pdf.

Subgroup members are also co-authors on the latest international standardised clinical follow-up guideline relating to survivors of childhood, adolescent and young adult cancer produced by the International Guideline Harmonization Group (www.ighg.org).

These achievements are best seen in context. The specific objectives of this Subgroup during 2018-21 have been:

- To undertake a systematic programme of national population-based cohort studies of survivors of TYA cancer to identify adverse health outcomes with substantially increased risk.
- To determine a comprehensive understanding of adverse health outcomes, using nested case-control studies to determine risk factors.
- To extend data linkage of the TYACSS cohort to additional new national electronic databases which become available.
- To study of new models of clinical survivorship care in high quality national research studies, in collaboration with the Germ Cell Tumour and Health Services Research Subgroups.
- To contribute to studies of fertility led by the main Research Group.

The progress against these objectives is listed in the time-specific table here:

Project	Lead individual	Others involved	Type	Milestone	Milestone Date	Output	Output date	Progress
Cerebrovascular Case-control study	Mike Hawkins	Children's Cancer and Leukaemia Group (CCLG) group	New	None	None	Funded	May-20	The Subgroup had formed a national study Advisory Group by May 2020
New TYACSS linkages	Mike Hawkins	None	New	Present possibilities for Fertility data linkage	Mar-19	New TYA risk stratification publication	2021	New risk stratification publication for TYA survivors being produced. Multiple new record linkages are currently underway.
Plan germ cell late effects analyses	Mike Hawkins	Germ Cell Tumour Subgroup	New	Agree key areas with Germ Cell Tumour Subgroup	Jan-19	New TYA risk stratification publication	2021	Although no exclusively GCT investigation undertaken the new TYA risk stratification publication is likely to be unprecedentedly informative for GCT survivors
Develop new models of follow up evaluation or trial	Danish Mazhar	Germ Cell Tumour Subgroup	Continuing	App partner agreed	Mar-19	Study design to Research Group	May-20	In development. Likely to restart after changes in services due to COVID-19. Multicentre Nursing PhD proposal in preparation 2021 (Leeds/Southampton) as a collaboration with the Germ Cell Tumour Subgroup

A new three-year grant from Children with Cancer UK began 1st January 2021 entitled: "Establish a comprehensive surveillance system for adverse health outcomes in British survivors of childhood, teenage and young adult cancer". The principal investigator is Prof Mike Hawkins. The value is £350,000. This grant includes a new collaboration with Dr Peter Hall, Edinburgh, to explore financial cost implications of surviving cancer using his health economic experience and that of his team.

Biological Studies Subgroup (Chair, Dr Sarah Pratap)

The specific aims of this subgroup are:

- Support and contribute to the development of studies that set out to understand age-specific tumour biology relevant to TYA cancer.
- Understand the age-specific host biology in TYA cancer.
- Facilitate personalised medicine in TYA with cancer.

The specific objectives of this group for this 12-month period to March 2021 were:

i. To build from Specta-AYA to biologically driven studies in relapsed TYA cancer.
ii. To support applications for a uniform UK biobanking infrastructure for TYA cancer.
iii. To develop a radiobiology study.

The progress of the subgroup against these in this reporting period has been:

i. Biologically driven study: A paper on AYA sarcoma diagnostic alterations due to genomic sequencing is in advanced draft. The biological platform is currently being optimised to be suitable for a wider study (rapid results and reliable nucleic acid extraction). A meeting to develop a detailed plan on molecular profiling between this Subgroup and the Health Services Research Subgroup has been delayed due to Lorna Fern's position changing.
ii. Biobanking: This is critical underpinning much of what this Subgroup wishes to achieve. An application to CRUK was reviewed by the TYA & GCT Group and submitted by the Newcastle group led by Prof Deb Tweddle and Owen Burbidge. Outcome is awaited. This would be timely as the NHSE service specification specifically mandates the offer of tumour banking, and there is a wider initiative ongoing in the groups that led the NHS GCIP processes to widen the collection of fresh tissue from testis tumours. The Subgroup is interested in exploring a 'count me in' approach to a future study, as in use in the US currently in rare cancers.
iii. Radiobiology: This trial has been in outline but the lead clinical oncologist has been unable to maintain capacity to do this work, due to COVID-19 NHS workload, and not been able to be replaced through requests to CTRad. Other approaches are being made. Due to the wider collaborations required this will go forward between the Biological Studies Subgroup and the main TYA & GCT Group.

There have been challenges:

i. A study on germline mutations in TYA cancer, led by Emma Woodward, Manchester, was rejected by the NIHR and is submitted in smaller form to the Little Princess Trust.
ii. A collaboration with the Wellcome Sanger Institute in Cambridge, to undertake the very deep genomic sequencing they undertake on TYA-onset carcinomas and compare to the same histological categories in older adults has not progressed as planned. The aim was to identify mutations that are actionable, now or in future, akin the work in SMPaeds with Roche. Initial linkage with Sam Behjati that was created was not workable due to his workload. The other researcher in that group put forward for this by Behjati did not

engage fully. We are seeking a collaboration with a different group in a different university. The ECMC work and widening of tumour banking might assist this further.

iii. Loss of the lead clinical oncologist for the radiobiology study.

These achievements are best seen in context. The specific objectives of this Subgroup during 2018-21 have been:

- To examine variations in radiobiology and pharmacology when cancer treatments are delivered in cohorts of patients of different ages.
- To design a stratified medicine trial in TYA with relapsed or refractory cancer, building upon the SPECTA EORTC initiative and evolution in Whole Genome Sequencing.
- To characterise and propose changes that may overcome barriers to the routine banking of tumour tissue at diagnosis or relapse in TYA with cancer.
- To explore the impact of dose intensity/toxicity on TYA patient outcomes.
- To undertake a change of Subgroup Chair.

We have made excellent progress against these objectives in 2020-21. Specifically, the following timed aims were set in 2018:

Project	Lead individual	Others involved	Type	Milestone	Milestone Date	Output	Output date	Current status
Personalised medicine studies	Martin McCabe	EORTC	Continuing	Meet including Next Generation Sequencing expert	Aug-18	Proposal for personalised medicine trial	May-21	SPECTA _AYA completed.
CCLG tissue bank	TBC	CCLG	Continuing	Qualitative data from CCLG centres	May-19	New study design	May-20	Funding applied for 2021 to bank tissue for all TYA up to 25 years.
Radiobiology and age	Dan Stark	CTRAD	New	New leadership group after workshop with CTRad	May-19	Protocol for TYA RT study	May-20	Stalled due to pulling out of clinical oncologist. Protocol in development - needs clinical oncology lead.
Pharmacology and age	Gareth Veal	Dan Stark, ECMC	New	Meeting with ECMC	Dec-18	Design for systematic review of PK and age	Dec-19	Recruitment completed - further funding applied for to do further analysis (Bone Cancer Research Trust[BCRT])
Dose intensity funded	Dan Stark	None	Continuing	Funding submitted to NIHR	Jan-19	None	None	Funding successful and study ongoing.
Identify new Chair for Subgroup	Dan Stark	None	New	None	none	New Chair in post	May-19	Dr Sarah Pratap appointed

Our QQR report 2021 serves to emphasise the priority that should be given to this Subgroup's work in the next 3 years strategy review. The reviewer's comment upon the need to focus more on clinical, translational and biological issues, and to define specific actions that could be taken to aid biobanking, working with wider clinical and biological stakeholders including disease-specific groups. Ironically a meeting to develop this has not proceeded due to the change of position of Lorna Fern.

New projects that have begun in this reporting period also:

i. A carboplatin study led from Birmingham in CNS germinoma 'Monogerm' is planned to examine vinblastine vs carboplatin in young people with CNS germinoma (a germ cell tumour of the brain). The aim is to limit ifosfamide exposure in chemosensitive disease, to minimise acute and late toxicity. There will be a 'flip flop' design for the phase 2 trial (John Apps) with the biological elements looking at micro RNA in CSF and serum. There is the opportunity to add in other biological aims at this point. This Subgroup aim to include an age specific question, such as the differential toxicity, doses delivered and response in pre- and post-pubertal individuals. Gareth Veal and Matt Murray are taking these biological questions forwards.
ii. AGCT 1531 (trial developed in Germ Cell Tumour Subgroup). There is great potential within this trial to include carboplatin pharmacokinetic data, across children and adults, alongside renal function and toxicity in UK patients who are included. This could address some of the debated, complex and incompletely studied issues raised in the design of 1531, about which individuals benefit from 'body surface area' and which 'area under the curve' approaches to carboplatin dosing.
iii. The impact of platinum dosing and adducts formed upon future fertility. There is a new collaboration between Gareth Veal and the Edinburgh group, with a link to the fertility study in development within the main TYA & GCT Group. Biological questions that aim to address the impact of chemotherapy on fertility are a priority for young people.
iv. There is a gap in the trials for tumours that were considered and managed as Ewing Sarcoma previously and are no longer, as they carry distinct specific mutations (e.g. Cic-Dux, BCOR). They have no standard of care, and for some the efficacy does not clinically justify the toxicity of using Ewing approaches. Within the new genomic landscape this has been flagged as an opportunity to collect nationwide data on this group of patients and start to understand the biology that underpins these rare diseases.

Health Services Research Subgroup (Chair, Dr Lorna Fern)

This Subgroup aims to:

- Develop and evaluate interventions which can improve recruitment of TYA to clinical trials and other high-quality research studies.
- Undertake research to improve routes to cancer diagnosis within the NHS.
- Evaluate specialist care for young people (aged 16-25 years) with cancer.
- Evaluate how e-health can improve cancer experience for young people.

The Subgroup has had a challenging year due to the impact of the COVID-19 pandemic on healthcare services and the research environment. Some members were redeployed to cover COVID-19 clinical duties, resulting in the premature departure of Consultant Nurse trainee Nicky Pettitt. Nicky had secured a noncancer specific role in her trust but had intended to finish her time with the Subgroup. However, she left early due to redeployment. Despite the numerous challenges we have continued with meetings, grant submissions and publications. We have had two online meetings with smaller group work in between. We have also rapidly mobilised our patient and public involvement work online, experimenting with different platforms, MIRO, secure

Zoom and Teams, and involving an artist Ben Connors to help us with translation of results. In total, we have held six online PPI meetings in the last reporting year, including an external collaboration with NHS DigiTrials.

Looking forward to 2021-22, the Health Services Research Subgroup now faces some instability as core members step down or retire. The dedicated research support for the NCRI TYA & GCT Group will cease at the end of this reporting year and Dr Fern will leave her current role as NCRI TYA researcher and PPI lead. In the interim period Dan Stark will look after the Subgroup between April 1st and end of May 2021. Dr Fern will then continue as Chair in her new role as TYA Health Services Researcher Senior Research Fellow based within UCLH Cancer Clinical Trials Unit. Pippa Simpson will join the Subgroup to join Max as our new Consumer. She already works on the STARS study and so is well placed to contribute to the work of the Subgroup. Sue Morgan will retire in April 2021 but will remain an honorary member of the Subgroup (join when agenda is relevant, while will still operate remotely). Sam Ahmedzai will step down in June 2021. We postponed our strategy meeting and membership refresh due to the pending structural changes of the Research Groups within the NCRI and the QQR feedback report. Following recent news that we will continue as a Subgroup (rather than a 'working party') for the next reporting period, a strategy meeting and membership refresh is planned for summer 2021.

The specific objectives of this group for this 12-month period to March 2021 were:

i. Ongoing evaluation of NHS services for TYA with cancer.
ii. The impact of TYA age on pathways to diagnosis.
iii. Use the JLA to influence funding.
iv. Develop and evaluate interventions which can improve recruitment of TYA to clinical trials and other high-quality research studies.

Progress against these has been:

i. Ongoing evaluation of NHS services for TYA with cancer

a. BRIGHTLIGHT (2011-19, £2.15m, awarded 2011):

Completion and dissemination of the BRIGHTLIGHT study is now achieved. This study was conceived in 2008, developed and implemented within the TYA Health Services Research Subgroup and is a manifestation of over a decade of work by the Group. The results of the primary and secondary outcome measure are published. The results raised some concerns within the TYA community and in order to fully inform practice and policy it was necessary to carry out further evaluation of TYA services.

Patient and public involvement - we held four online workshops supported by Ben Connors the artist to help with interpretation of the results for our young advisory panel of which Max is part of.

b. BRIGHTLIGHT_2021 (~150K, awarded 2020)

Group involvement - Joint Principle Investigators Dr Lorna Fern & Dr Rachel Taylor; Professor Dan Stark; Dr Richard Feltbower; Dr Martin McCabe. The purpose of BRIGHTLIGHT_2021 is to determine if there are differences in outcomes for young people with cancer receiving 'joint care' between the Principal Treatment Centre (PTC) or the equivalent in Scotland and Wales and networked hospitals, compared to those who have all or no care in a TYA-PTC.

The project outcomes are quality of life, survival, and experience of cancer care.

The aims and objectives of the whole programme are to:

1. Determine if clinically significant differences exist in outcomes for TYA receiving joint care compared to all or no-TYA-PTC care in 2021.
2. Explore the processes used to enable inter-organisational collaboration under joint care models.

3. Determine the outcomes associated with joint care and how they may be optimised.

BRIGHTLIGHT_2021 is a mixed methods study, we aim to recruit 500-700 young people newly diagnosed with cancer in 2021 and rapid ethnography of the delivery TYA cancer care across the UK during the same time period. We have deferred recruitment due to COVID-19 and are now aiming to start recruitment on August 1st 2021. The eligibility criteria for BRIGHTLIGHT_2021 is broad so the majority of young people will be eligible to participate.

Patient and public involvement - we held two online workshops updating the BRIGHTLIGHT survey. Two members of the young advisory panel are members of the BRIGHTLIGHT_2021 steering group.

c. STARS: 2019-22 (£1m, previously known as 'ESRC social integration', awarded 2019)

Group involvement: Principle Investigator Professor Dan Stark, Dr Rachel Taylor; Dr Louise Soanes; Ms Sue Morgan. This is a mixed-methods analysis, pooling existing general population data, existing cancer-specific data on TYA within BRIGHTLIGHT, and a new cohort of 524 people aged 16-39 living with and after cancer. The aim is to describe the impact of cancer upon the trajectory of social outcomes (specifically education, work/training and social networks) in young people.

Objective 1. Study 1: To understand which socio-demographic factors explain differences in social integration trajectories in young people aged 16-39 with and without cancer. We will use the British Household Panel Survey and the UK Household Longitudinal Study databases (Understanding Society). This forms a 'counterfactual' against which we will compare merged data from Studies 2 and 3

Objective 2. Study 2. To explain which clinical factors influence social reintegration trajectories in young people with cancer, over and above socio-demographic factors in the 3 years after cancer is diagnosed. This second study involves the secondary data analysis of the National Institute of Health Research-funded 2014-19 BRIGHTLIGHT cohort study.

Objective 3. Study 3. To identify which other factors (patient-reported outcomes, psychosocial factors, and emerging factors) further explain social reintegration differences in young people diagnosed with cancer. We will undertake a prospective longitudinal questionnaire study, with a qualitative sub-component, in two cohorts of people aged 16-39, purposively sampled across two major cancer centres in Yorkshire and London. This will include recently diagnosed patients and long-term survivors, each sampled at 2 timepoints.

This study, as a chance by-product of its timing, also permits a prospective mixed-methods examination of the impact of COVID-19 on this patient group. The study is approved by ethics and by the NIHR for portfolio adoption, data for Study 1 is undergoing analysis, data for Study 2 is under analysis, and Study 3 is recruiting in both centres despite the COVID-19 context.

Patient and public involvement - Eight workshops have been completed with a study-specific Patient and Public Voice group, who have contributed to the questionnaire design, branding and recruitment to the study and are now receiving ongoing research training while data accrues.

ii. The impact of TYA age on pathways to diagnosis

REFER_ME/CRUK study (40K, awarded 2019)

Group involvement: Principle Investigator: Dr Lorna Fern; Professor Jeremy Whelan (Co-Applicant); Dr Rachel Taylor (Co-Applicant); Faith Gibson (former member). Patient recruitment; secondary analysis of BRIGHTLIGHT, n=830

Aim: To identify clinical and patient reported outcomes associated with diagnostic and treatment pathways.

We are delighted to report this grant has been successfully implemented and analysis has been completed. The paper has been submitted to the Lancet Oncology in the first instance and shows patient reported outcomes associated with diagnostic intervals which has not been reported previously either in TYA or older adults. The Group are grateful for the diligent and rapid progress of the analyst Dr Alice Forster, UCL.

We published our pre-diagnostic symptoms work in JAMA open which has been viewed 1698 times.

Patient and public involvement We held two online PPI workshops to guide analysis and for interpretation of results.

iii. Using the JLA to achieve funding

This has been more challenging this year due to the COVID-19 pandemic. However, we have completed analysis of the free text and this is currently under review with health expectations. The paper provides details of information and support gaps for TYA.

Patient and public involvement: The young people on the steering group are co-authors on the paper. We also completed an independent evaluation of the impact of working on the JLA for the young people involved. This was carried out by TwoCan Associates and can be viewed here:

http://www.twocanassociates.co.uk/wp-content/uploads/2020/05/An-evaluation-of-young-peoples-involvement-in-the-Teenage-and-Young-Adult-Cancer-JLA-PSP-May-2020.pdf

iv. Develop and evaluate interventions which can improve recruitment of TYA to clinical trials and other high-quality research studies

We submitted a programme development grant to further develop the 5As model we published in the Lancet Oncology in 2014. The 5As are also integral to the ECMC project (see cross-cutting main Research Group, above)

Patient and public involvement; We have co-hosted an online workshop with NHS Digi-trials.

These achievements are best seen in context. Progress against our 2018-21 objectives is below:

Project	Lead individual	Others involved	Type	Milestone	Milestone Date	Output	Output date	Progress to date
Use the JLA to influence funding	Lorna Fern	The JLA leads	New	Meet with funders	Nov-18	Meeting with charity funders	Nov-19	Completed May 2020. We also completed an independent evaluation of the impact of working on the JLA for the young people involved. This was carried out by TwoCan Associates and can be viewed here: http://www.twocanassociates.co.uk/wp-content/uploads/2020/05/An-evaluation-of-young-peoples-involvement-in-the-Teenage-and-Young-Adult-Cancer-JLA-PSP-May-2020.pdf
Ongoing evaluation of NHS services for TYA with cancer	Rachel Taylor	BRIGHTLIGHT	Continuing	Commence a PhD student examining the longer follow-up data	May-19	Use BRIGHTLIGHT data to inform NHS England service specifications	May-21	Completed - BRIGHTLIGHT study disseminated. Funding secured for BRIGHTLIGHT_2021 to validate findings ahead of any NHS service changes.
The impact of TYA age on pathways to diagnosis	Lorna Fern	none	Continuing	Include systems research and logic modelling in the Heath Services	May-19	Present the designed programme to the main Research Group.	May-20	Completed funding from CRUK secured and completed. Outcomes with prolonged pathways identified.

				Research Subgroup				
Evaluate the impact of a change in TYA research structures	Lorna Fern/Rachel Taylor	TCT, NCRI, NIHR	New	Include systems research and logic modelling in the Health Services Research Subgroup	Jul-19	Present the designed evaluation to the main Research Group	Jul-20	Project completed but intervention not put in place by NIHR to study. Now progressing via informal means.

The Chair would like to thank the Subgroup for their ongoing work despite the COVID-19 pandemic and support over the past year. To meet the challenges of the post-pandemic world, and prior to membership refresh, we conducted an online survey of the Group of ways of working. Feedback favoured more frequent shorter meetings. We will now move to shorter meeting every 8 weeks online rather than twice yearly three/four-hour meetings. This will begin in ~June 2021.

4. Cross-cutting research

The projects noted above in Fertility, PPIE, Experimental Cancer Medicines for TYA and digitally supported follow-up are cross-cutting in that they bring together the Germ Cell Tumour, Biological Studies and Quality of Life & Survivorship Subgroups. We have an early survey of unmet needs work ongoing with the NIHR Nutrition and Cancer collaborative specific to TYA with cancer.

We have one working party ongoing: EARLY ONSET CARCINOMA working party.

We are particularly pleased with progress this year. The initial research idea was identified by Dr Angela Jesudason as TYA & GCT Group co-chair in 2016, and then was refined with Richard Feltbower, Martin McCabe and colleagues from Addenbrooke's, Southampton, UCLH and Warwick. Under new leadership from Dr Richard Feltbower, the working party will address the lack of epidemiological data on early onset carcinoma. In particular, we wish to evaluate the clinico-pathological features of early onset breast, colorectal and ovarian carcinoma to inform the development of treatment and management strategies and improve outcomes among those diagnosed between the ages of 16-39 years.

Aims:

- To identify and characterise the clinical features of carcinomas developing in those aged under 40 in the UK.
- To develop collaborations between the TYA and site-specific Groups.
- To develop a study proposal in patients developing carcinomas aged under 40.
- To interrogate the enhanced cancer registry to determine the UK epidemiology, available treatments and outcomes for Ovarian, Breast and Colorectal Carcinomas diagnosed aged under 40 years.
- To interrogate UK tumour banks and existing clinical trials cohorts to determine their coverage of the range of biology in this same patient group.
- To apply for funding for further research in this field

The key successes of the working party in this reporting period have been:

A data request application was successful to the Office for Data Release and in Spring 2020 we agreed a de-identified extract to meet data anonymisation and ethics approvals. Governance approval was provided by the Office of Data Release Caldicott Guardian in June 2020 with confirmation that no formal ethical approval was required given the de-identified nature of the data requested.

Agreement of the relevant morphology codes took place between July-September and a contract and Data Sharing Agreement signed in November. The data extract was received in December and started statistical analysis in January 2021. The robust links with the National Cancer Registration and Analysis Services (NCRAS) and PHE who are facilitating the data extract will prove very useful in this project and future health services research. The successful development of links with breast, colorectal and ovarian tumour oncologists with an interest in young-onset cancer will promote future clinical collaborations.

Initial descriptive analyses are exciting, hinting at distinct patterns of differential outcomes by age among early-onset carcinomas, and stimulating widespread enjoyable debate among the investigators. The study has considerable large potential in future, evaluating existing UK clinical trials data extending down to TYA age range and comparing long-term outcomes vs older adults (15-39, 40+) for breast, colorectal, ovarian and GCTs

5. Funding applications in last year

Table 1 Funding submissions in the reporting year

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
March 2021					
Unravelling the chronological history of high-risk Paediatric SARComas and the dynamics of progression and relapse/ PaedSARC	Cancer Grand Challenge (Expression of Interest)	Burchill (previous CSDG member), with Stark and others	Awaited	Collaborator	£20 million
Clinical and Patient Reported Outcomes associated with multiple GP consultations and pre-diagnostic intervals for teenagers and young adults with cancer: secondary data analysis of the BRIGHTLIGHT Cohort	CRUK EDAG	Lorna Fern	Awarded 2020	Driven from this Research Group (Health Services Research Subgroup)	£41,209
rEECur: International Randomised Controlled Trial of Chemotherapy for the Treatment of Recurrent and Primary Refractory Ewing Sarcoma	CRUK CRC March 2021 committee	Martin McCabe / Keith Wheatley	Successful	BSG reviewed and discussed trial design. Formal input by TYA Germ Cell Tumour Subgroup. Biological sample collection embedded	£850,305.48. (Final funding amount unclear)
BRAINatomy: a validated anatomical atlas of childhood neuroradiation damage	Stand Up 2 Cancer / CRUK Pediatric Cancer New Discoveries Challenge	Martin McCabe	Successful	Discussed in relation to Biological Studies Subgroup radiobiology project. Imaging biomarker studies are integral. Germline predisposition substudy is being prepared.	USD 999,781
Other committees**					

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Developing an evidence-based psychoeducational intervention for teenagers and young adults who have retinoblastoma. PhD Studentship	CHECT (CHildhood Eye Cancer Trust)	PI- Bob Phillips	Funded	Collaboration with Biological Studies Subgroup members	£73,799 (POSTPONED FOR COVID-19) `
Chaplaincy services and the spiritual care and support needs of children and young people, and their parents, facing end of life,	NIHR HS&DR Reference Number: NIHR128468	CoI- Bob Phillips, , with Bryony Berrisford	Funded	Collaboration with Biological Studies Subgroup members	£467,835 from 2020 for 2 years
End of Life Care for Infants, Children and Young People: a mixed methods evaluation of current practice in England and Wales.	NIHR HS&DR Reference Number: NIHR129213	CoIs- Bob Phillips, Richard Feltbower, with PI Lorna Fraser	Funded	Collaboration with Biological Studies Subgroup members	CoI, £1,196,569.95 from Sept 2020 for 4 years
Understanding treatment decision-making processes in families where a child or young person has relapsed/refractory rhabdomyosarcoma.	CCLG Special Named Funds	PI- Bob Phillips	Funded	Collaboration with Biological Studies Subgroup members	£96,199.89 from March 2021 for 18 months
Using microRNA 371 to better define which Stage 1 non-seminomatous germ cell tumour (NSGCT) patients can safely avoid adjuvant BEP chemotherapy.	RM BRC is the funder.	PI- Alison Reid	Funded	Collaboration Germ Cell Tumour and Biology Studies Subgroups.	£19,200. One year.
Exploratory Study of Molecular Characterisation in Patients with Metastatic Germ Cell Tumours Refractory/Resistant to Platinum Treatment (EMIT).	BRC is the funder. PI.	PI- Alison Reid	Funded	Collaboration Germ Cell Tumour and Biology Studies Subgroups.	£20,000. One year
Optimising the Treatment of Teenagers and Young Adults with Ewing Sarcoma through an Increased Understanding of Clinical Pharmacology and Toxicity Biomarkers	Bone Cancer Research Trust translational grant	G. Veal	Awaiting decision	Developed from strategy	£146,280

Epigenomic translocations: a mechanism of oncogene deregulation in T-cell acute lymphoblastic leukaemia. Co-investigator - Gareth Veal	JGWP – pilot grant (1 year)	Lisa Russell	Funded	Developed with Biology Studies Subgroup.	£49,900
Optimising the use of repurposed drugs to improve the treatment of children with ALL. Co-investigator Gareth Veal	Children with Cancer – 3 year project grant	Julie AE Irving	Funded	Developed within Biology Studies Subgroup.	£49,900
Funding to investigate regorafenib in phase II/III randomised study in relapsed rhabdomyoasarcoma within FaR-RMS study to generate data for PIP filing.	Bayer pharmaceuticals, CRUK Clinical Trials Unit, University of Birmingham	Dr Meriel Jenney Chief Investigator Dr Julia Chisholm Joint Lead	Funded	Developed with collaboration of main Research Group.	£22,000,000 over 5 years
CO-LENVA: A multi-centre, open-label, non-randomised phase Ib study of the toxicity and safety of the Combination of LENVAtinib with the chemotherapy regimens topoten-cyclophosphamide, carboplatin-etoposide and ifosfamide in children and young adults with recurrent or refractory solid tumours.	Fight Kids Cancer early phase clinical trials grant	Martin McCabe (Biology SG)	Awaited	BSG aware of trial. Formal input by TYA Germ Cell Tumour Subgroup. Biomarker studies embedded	€1,388,950.93
Liquid Biopsies to Support Management of Ewing Sarcomas.	Friends of Rosie project grant	Caroline Dive (McCabe co-I)	Successful	Discussed by the Group. Submission not formally reviewed	£75,427
What clinical outcomes are associated with the 'joint care' proposed by NHS England for Teenagers and Young Adults with cancer? BRIGHTLIGHT -2021	NIHR Policy Research Programme Call for Applications	Dr Rachel Taylor Dr Lorna Fern	Successful	Developed from strategy	£149,770
RECRUIT_ME: a programme to develop and test interventions to improve recruitment of teenagers	NIHR Programme Development Grant	Dr Lorna Fern Dr Rachel Taylor	Under review	Developed from strategy	£138,383

and young adults to cancer clinical trials					

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Clinical Pharmacology Studies to Optimise the Treatment of Teenagers and Young Adults with Ewing Sarcoma	Sarcoma UK PhD Studentship application	G. Veal	Not funded	Developed from strategy	£118,289
'CO-creating adolescent Resilience to Adversity: a whole systems approach to improve mentaL health - The CORAL programme'	MRC/AHRC/ESRC Adolescence, Mental Health and the Developing Mind	Darlington (HSR SG) with Stark	Not funded	Discussed in Health Services Research Subgroup.	£3,955,143
Establishing the prevalence of hereditary alterations in cancer predisposition genes in the teenage and young adult (TYA) cancer population - implications for the TYA individual, their family and the NHS.	NIHR advanced fellowship	Dr Emma Woodward PI	Not funded	Developed from strategy	
A clinically integrated intervention for addressing psychological distress and treatment adherence together, during the cancer care of Teenager and Young Adults.	NIHR Programme Grant	Professor Dan Stark	Unsuccessful at stage 2	Developed from Strategy	
RELAY_ME BRIGHTLIGHT research to practice: Informing teenage and young adult cancer care services to maximise outcomes (RELAY_ME)	NIHR Programme Development Grant	Dr Rachel Taylor Dr Lorna Fern	Unsuccessful at stage 1	Developed from BRIGHTLIGHT	£142,395

**CRUK CRC applications for table 1 completed by NCRI Executive.*
***Other applications in the table to be completed by Group Chair*

6. Consumer involvement

Max Williamson

Positively, this year, the NCRI TYA & GCT Research Group held an essential role within the NCRI with regards to Consumer Involvement. Our work has maintained a high profile for the Research Group throughout the UK and the wider research community. Max Williamson has maintained effective connections with teenage and young adult cancer research groups ranging from the NIHR TYA Clinical Research Network Steering Group and NHS England's Fertility Preservation Program to beginning work with the Genomics England Testis Group. In the last year, this work expanded to multiple funding committee contributions for Cancer Research UK, including an ad-hoc review for paediatric, TYA & GCT and brain tumours for the CRUK Clinical Research Committee (CRC) in July 2020 to reassess funding given the impact of COVID-19 on the charity. He continues his role as patient representative on three trial management groups on the Research Group's clinical trial portfolio: TIGER, P3BEP and AGCT1531. In terms of international work, Max supports the ACCELERATE FAIR Trials group with their work, including the development of a toolkit to support patients and parents advocate for change with regard to exclusionary trial age limits. He also joined the Malignant Germ Cell International Consortium as a patient representative in October 2020 and completed the European Patient Forum's Summer Training Course in Youth Participation and Advocacy in November 2020, working with young people across disease groups and European nations to develop youth health advocacy projects. Vince Wolverson has now completed his tenure with the NCRI TYA & GCT Research Group and maintains his strong involvement with local testicular cancer charities across the UK; his local charity 'It's On the Ball' continues to support youth education around testicular cancer throughout East Anglia. We thank him immensely for his support of and contributions to the Research Group over the last six years.

Sadly, this year also saw the loss of two key members of the Research Group with regard to Consumer involvement. In June 2020, Lara Veitch died. She was a wonderful presence to have on the Group, in her contributions to research, in her recognition of the wider cancer community, and in her manner and character. During her time with the Research Group, she contributed immensely to its' portfolio, including membership of the Health Services Research (HSR) Subgroup and being a key member of the JLA Teenage and Young Adult Priority Setting Partnership Steering Group. In 2017, she presented her work on teenage and young adult cancer patient's view of tissue banking as a poster at the NCRI Conference, and then moved to co-produce and inspire the internationally acclaimed Stage-show 'A Pacifist's Guide to the War on Cancer'. She was a superb, enduring presence with the Research Group, and she will be missed. Over many years Dr Lorna Fern has been a magnificent champion for TYA Cancer Consumer engagement within the NCRI TYA & GCT Group and the wider NCRI, integrating Consumer work into the wider clinical research community, identifying, promoting and delivering opportunities for ever stronger consumer engagement, including support and informal guidance for the young people taking par through thick and thin. Any success we have had in this are substantially due to her work. Unfortunately, Lorna's time in this role came to an end this year. We believe we have found a way within the academic community to maintain Lorna as a researcher in this field. The role of champion and lead for delivery of these vital aspects of our research now moves to others, within the NCRI, who we hope will have the time to maintain our momentum. There is a risk this removal of the role Lorna was in by the NCRI, supporting the PPIE carried out and innovating in that, results to an expectation the support for PPIE will be delivered largely by the Group Chairs themselves, in direct competition with their clinical and wider research leadership roles. We would expect if that happened, this would be less successful for the PPIE and therefore for the research completed.

Returning to a positive note, we have the privilege of welcoming an increasing number of new young voices as Consumers on the Group. Five new Consumers, Emma Williams, Pippa Simpson, Bethany Mickleburgh, Josh Henderson and Kyle Blain will join the Group, and expand Consumer representation within each of the TYA & GCT Subgroups. This work has already begun: four Consumers took part in a patient engagement review of the PROTECT fertility study in April 2021,

contributing to the study design and construction with the support of the Research Group's Chair Dan Stark. Future projects, including a new venture looking to widen access to research engagement for any young person with cancer called the UK Youth Cancer Forum (attached as addendum), will illustrate how much the TYA & GCT has left to contribute to PPI within the NCRI network, on top of what Lara, Lorna, Max, Dan and Vince have contributed over the last year.

7. Collaborative partnership studies with industry

We have built the fertility study upon industry funded pump-priming. We plan to build an industry collaboration into the PhD to study technology-supported follow-up in Germ cell tumours - a new collaboration between the Quality of Life & Survivorship and the Germ Cell Tumour Subgroups, Leeds and Southampton with others. We plan a collaboration with industry within the Biological Studies Subgroup, around targeted therapies at relapse.

8. Priorities and challenges for the forthcoming year

Priority 1 To develop a new strategy for 2021-2024. We have had to wait some while due to NCRI restructure and await a specific date to meet in September 2021.
Priority 2 To invest resources and time, with the support of the NCRI, to move our specific programme of biological and translational research such that specific new prospective studies are in place, as advised by our QQR report.
Priority 3 To invest resources and time, with the support of the NCRI, to build upon our success and develop an expanded programme of LWBC studies, as advised by our QQR report.
Challenge 1 To continue our ambitious programme of patient and public engagement we with the marked reduction in investment of dedicated time for this element of our work.

Dr Dan Stark (TYA & GCT Group Chair)

Appendix 1

Membership of the TYA & GCT Main Group

Name	Specialism	Location
Dr Ben Fulton	Clinical Oncologist	Glasgow
Dr David Cutter	Clinical Oncologist	Oxford
Prof Mike Hawkins	Epidemiologist	London
Dr Richard Feltbower	Epidemiologist	Leeds
Dr Anna Castleton	Haematologist	Manchester
Dr Ben Carpenter	Haematologist	London
Dr Lorna Fern	Health Services Researcher	London
Dr Dan Stark	Medical Oncologist	Leeds
Dr Sarah Pratap	Medical Oncologist	Oxford
Dr Alison Reid	Medical Oncologist	London
Dr Matthew Murray	Medical Oncologist	Cambridge
Dr Naveed Sarwar	Medical Oncologist	London
Dr Paul Chumas	Neurosurgeon	Leeds
Dr Louise Soanes	Nurse	London
Dr Sara Stoneham	Paediatric Medical Oncologist	London
Dr Julia Chisholm	Paediatric Medical Oncologist	London
Dr Amos Burke	Paediatric Medical Oncologist	Cambridge
Dr Angela Jesudason	Paediatric Medical Oncologist	Edinburgh
Dr Adam Glaser	Paediatric Clinical Oncologist	Leeds
Mrs Carla Reid	Physiotherapist	London
Dr Graham Wheeler	Statistician	London

Consumer Representation

Name	Location
Mr Max Williamson	Oxford, UK

Trainee Members

Name	Specialism	Location
Hadeel Hassan	Clinical Research Fellow	Leeds, UK

Membership of the Subgroups

Health Services Research Subgroup		
Name	**Specialism**	**Location**
Dr Rachel Taylor	Associate Professor of Nursing	London
Mr Max Williamson	Consumer	Oxford
Dr Lisa McCann	Health Services Researcher (Digital)	Strathclyde
Dr Dan Stark	Medical Oncologist	Leeds
Dr Rachel Dommett	Paediatric Haematologist	Bristol
Prof Sam Ahmedzai	Palliative Medicine	Sheffield

Dr Anne-Sophie Darlington	Professor of Psychological Health	Southampton
Dr Lorna Fern (Chair)	Teenage and Young Adult Health Services Researcher, PPI expert	London
Ms Sue Morgan	TYA Consultant Nurse	Leeds

Quality of Life and Survivorship Subgroup		
Name	**Specialism**	**Location**
Dr David Cutter	Clinical Oncologist	Oxford
Ms Bethany Mickleburgh	Consumer	London
Mr Max Williamson	Consumer	London
Prof. Mike Hawkins (Chair)	Epidemiologist	Birmingham
Dr Raoul Reulen	Epidemiologist	Birmingham
Prof Dan Stark	Medical Oncologist	Leeds
Dr Danish Mazhar	Medical Oncologist	Cambridge
Dr Bethan Ingram	Nurse Practitioner	Cardiff
Prof Hamish Wallace	Paediatric Oncologist	Edinburgh
Mrs Carla Reid	Physiotherapist	London
Dr Gemma Pugh	Social Scientist	London

Germ Cell Tumour Subgroup		
Name	**Specialism**	**Location**
Dr Alison Reid	Medical Oncologist	London
Dr Jonathan Shamash	Medical Oncologist	London
Dr Andrew Protheroe	Medical Oncologist	Oxford
Dr Naveed Sarwar	Medical Oncologist	London
Dr Constantine Alifrangis	Medical Oncologist	London
Dr Matthew Wheater	Medical Oncologist	Southampton
Dr Sara Stoneham	Paediatric Medical Oncologist	London
Dr Clare Verrill	Pathologist	Oxford

Biological Studies Subgroup		
Name	**Specialism**	**Location**
Dr Clare Rowntree	Haematologist	Cardiff
Dr Matthew Murray	Lecturer	Cambridge
Dr Sarah Pratap	Medical Oncologist	Oxford
Dr Lorna Fern**	Medical Oncologist	London
Dr Dan Stark	Medical Oncologist	Leeds
Dr Frederik Van Delft	Medical Oncologist	Newcastle
Dr Angela Jesudason	Paediatric Medical Oncologist	Edinburgh
Dr Bob Phillips	Paediatric Medical Oncologist	York
Dr Christopher Barton	Paediatric Medical Oncologist	Liverpool
Dr Maria Michelagnoli**	Paediatric Medical Oncologist	London
Dr Rachael Windsor**	Paediatric Medical Oncologist	London
Dr Shaun Wilson	Paediatric Medical Oncologist	Oxford
Dr Gareth Veal	Pharmacologist	Newcastle

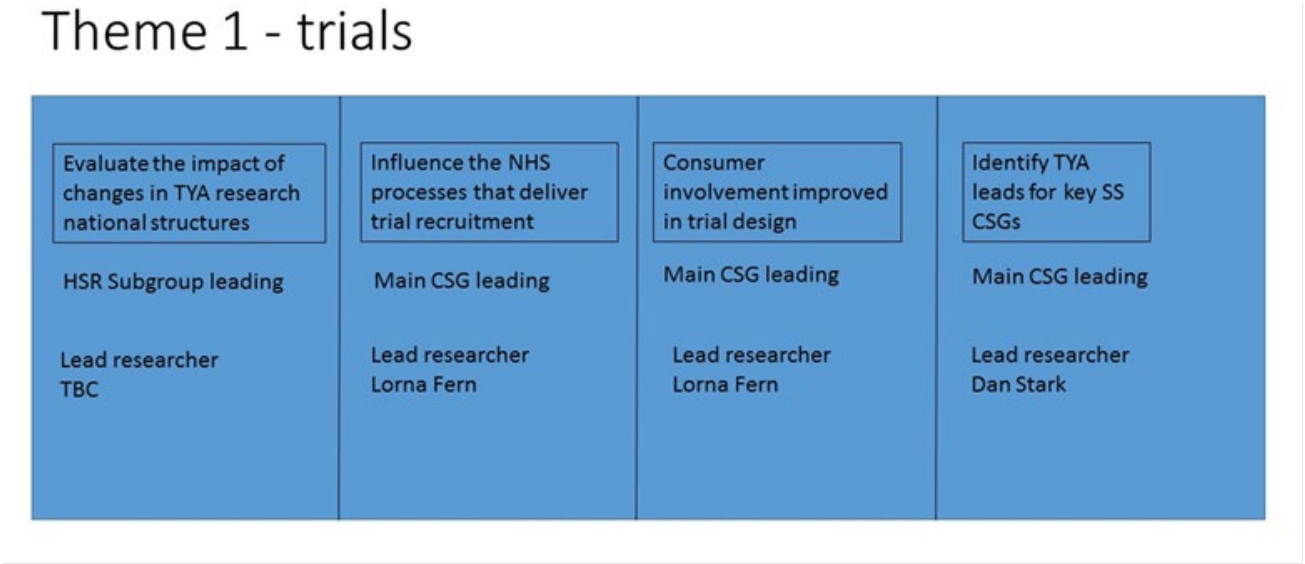
Mr Kenneth Rankin	Surgeon	Newcastle

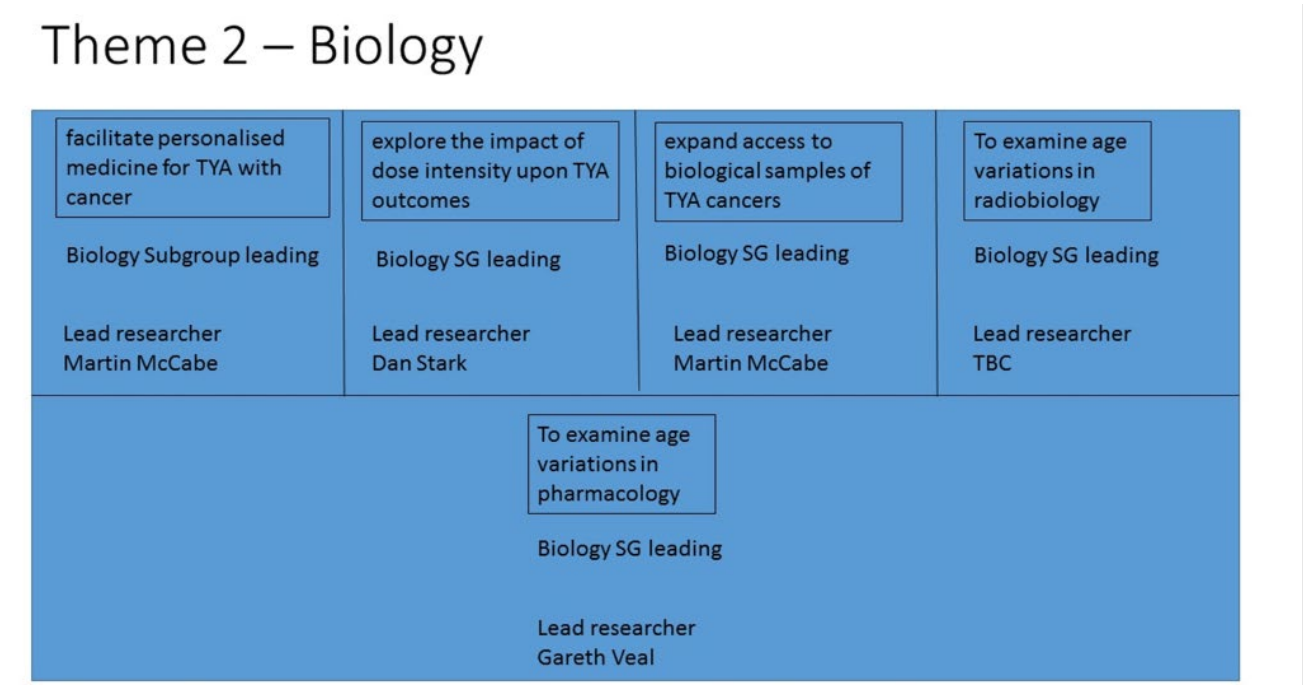
* denotes trainee member
**denotes non-core member

Appendix 2

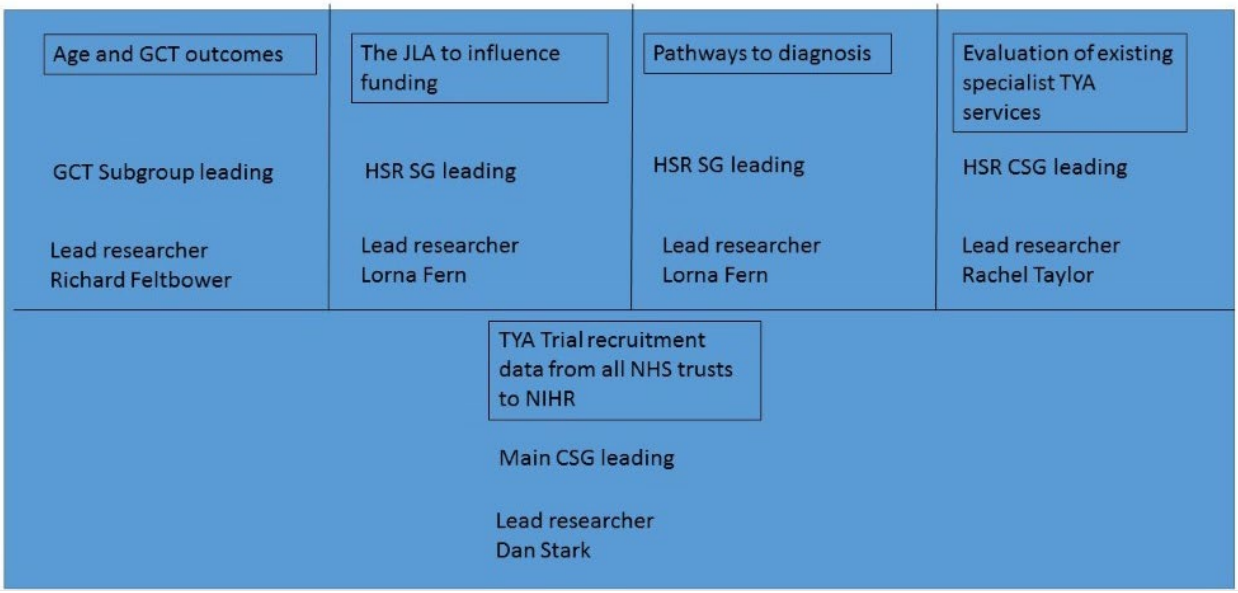
TYA & GCT Group & Subgroup Strategies

Themes aim to consolidate the objectives of the cross-cutting main Group and our Subgroups, and also to promote cross-subgroup working. Below are simple visual summaries of these themes, as they were generated in 2018. Progress towards strategic objectives can be seen in Section 3.

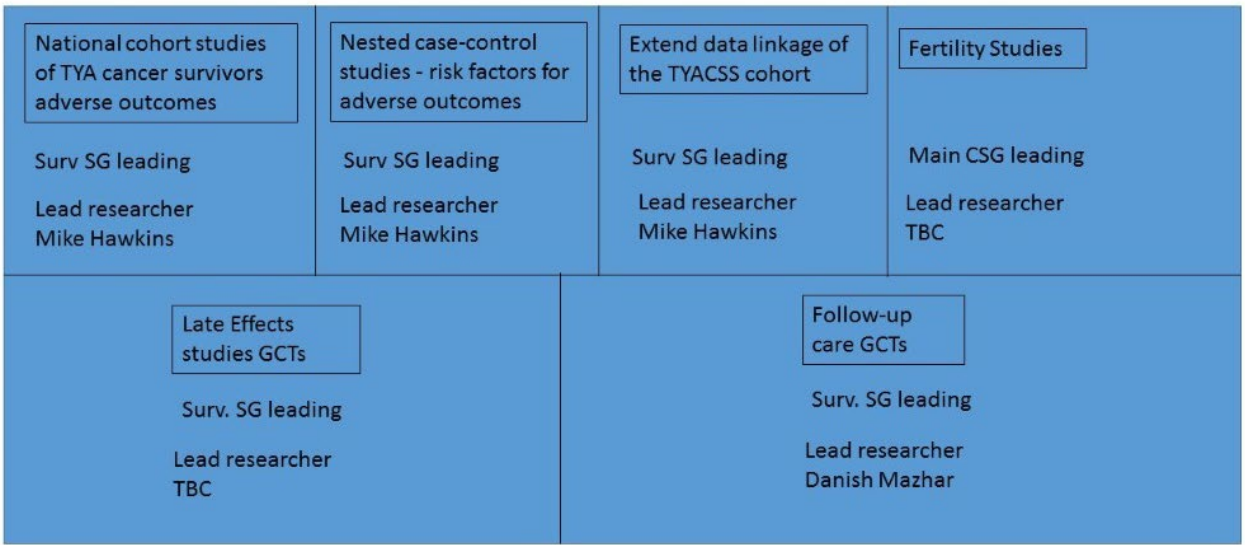




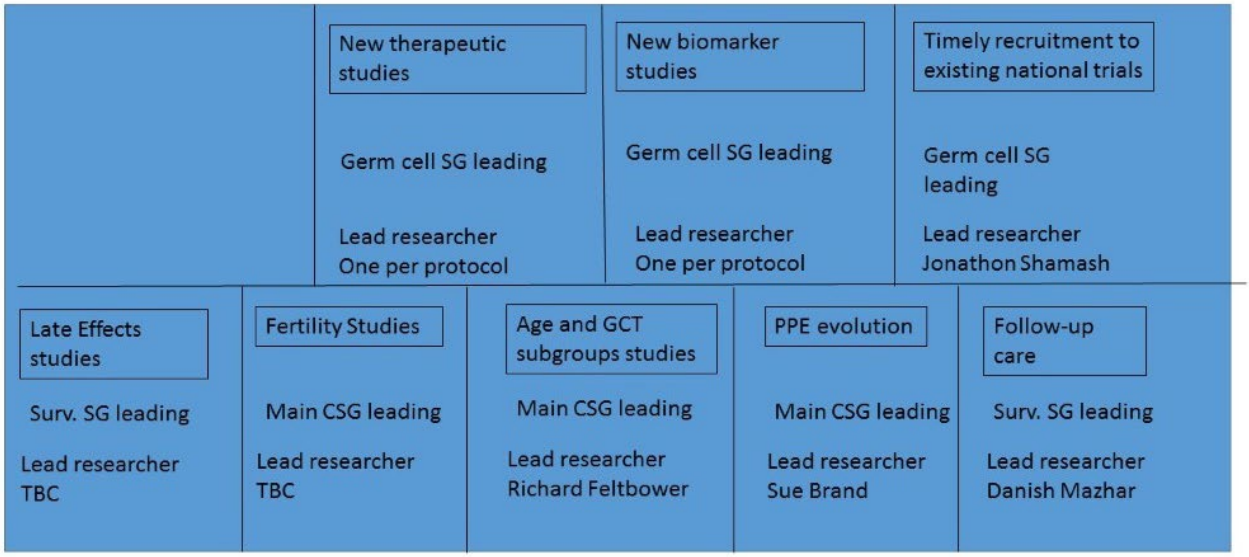
Theme 3 – Healthcare Provision



Theme 4 – Survivorship

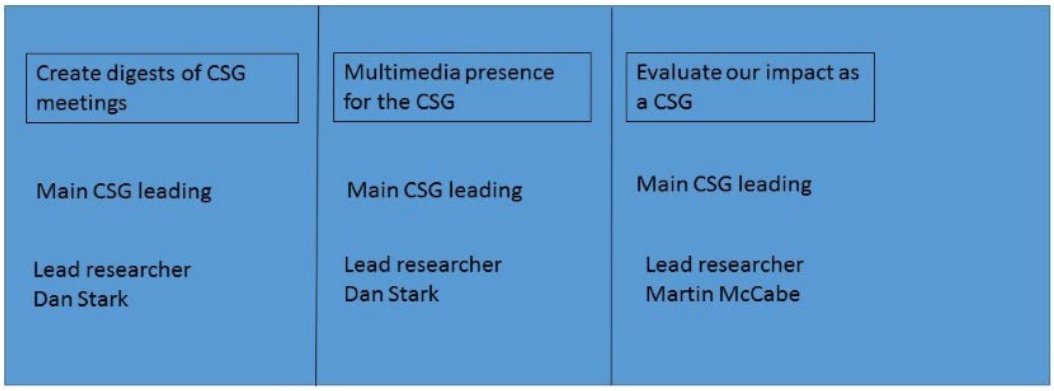


Theme 5 - GCTs



Theme 6 – Joint working

Theme 7 – Impact



Appendix 3

Strategic and/or high impact publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. Ci B, Lin S-Y, Yao B, Luo D, Xu L, Krailo M, **Murray MJ**, Amatruda J, Frazier A, Xie Y. Developing and using a data commons for understanding the molecular characteristics of germ cell tumors. Protocol Chapter. Editor: Aditya Bagrodia and James Amatruda. Title: Testicular Germ Cell Tumors. Methods in Molecular Biology, 2021; 2195:263-275. ISBN 978-1-07-160860-9.	AGCT 1531 – moving forward global contributions and analysis of germ cell tumour biology	Co-Leading the trial from the Germ Cell Tumour Subgroup. Leading the biology from the Biology Studies Subgroup. Note also Ci B, Yang D, Krailo M, Xia C, Yao B, Luo D, Zhou Q, Xiao G, Skapek SX, **Murray MJ**, Amatruda JF, Klosterkemper L, Shaikh F, Faure-Conter C, Fresneau B, Volchenboum S, **Stoneham S**, Nicholson JC, Lopes LF, Frazier LA, Xie YN. Development of Data Models and Data Commons for Germ Cell Tumors. Journal of Clinical Oncology Clinical Cancer Informatics, 2020;4:555-566. And Lafin JT, Singla N, Woldu S, Lotan Y, Lewis CM, Majmudar K, Zhou M, Kapur P, Margulis V, **Murray MJ**, Amatruda JF, Bagrodia A. Serum microRNA-371a-3p levels predict viable germ cell tumor in chemotherapy-naïve patients undergoing retroperitoneal lymph node dissection. European Urology, 2020;77:290-292.
2. 111 trial. Cullen M, **Huddart R, Joffe J**, Gardiner D, Maynard L, Hutton P, **Mazhar D, Shamash J, Wheater M**, White J, Goubar A, Porta N, Witts S, Lewis R, Hall E; 111 Trial Management Group. The 111 Study: A Single-arm, Phase 3 Trial Evaluating One Cycle of Bleomycin, Etoposide, and Cisplatin as Adjuvant Chemotherapy in High-risk, Stage 1 Nonseminomatous or Combined Germ Cell Tumours of the Testis. Eur Urol. 2020 Mar;77(3):344-351. doi: 10.1016/j.eururo.2019.11.022.	Reduction in chemotherapy required for young people with germ cell tumours	Designed and implemented in this Research Group and its predecessor
3. Loveday C, Litchfield K, Proszek PZ, Cornish AJ, Santo F, Levy M, Macintyre G, Holryod A, Broderick P, Dudakia D, Benton B, Bakir MA, Hiley C, Grist E, Swanton		

C, **Huddart R**, Powles T, Chowdhury S, Shipley J, O'Connor S, Brenton JD, **Reid A**, de Castro DG, Houlston RS, Turnbull C. Genomic landscape of platinum resistant and sensitive testicular cancers. Nat Commun. 2020 May 4;11(1):2189. doi: 10.1038/s41467-020-15768-x.		
4. **Murray MJ**, Smith S, Ward D, Verduci L, Nicholson JC, Scarpini CG, Coleman N. Circulating microRNAs as biomarkers to assist the management of the malignant germ cell tumour subtype choriocarcinoma. Translational Oncology, 2021;14:100904.	AGCT 1531 – moving forward global contributions and analysis of germ cell tumour biology	Co-Leading the Trial form the Germ Cell Tumour Subgroup. Leading the biology from the Biology Studies Subgroup
5. Clements C, Cromie KJ, Smith L, **Feltbower RG,** Hughes N, **Glaser AW**. 2020. Risk stratification of young adult survivors of cancer to estimate hospital morbidity burden: applicability of a pediatric therapy-based approach. *Journal of Cancer Survivorship*.		
6. Shaikh F, Stark D, Fonseca A, Dang H, Xia C, Krailo M, Pashankar F, Rodriguez-Galindo C, Olson TA, Nicholson JC, Murray MJ, Amatruda JF, Billmire D, Stoneham S, Frazier AL. Outcomes of adolescent males with extracranial metastatic germ cell tumors: a report from the Malignant Germ Cell Tumor International Consortium. Cancer, 2021 Jan 15;127(2):193-202. doi: 10.1002/cncr.33273. Epub 2020 Oct 20.	MAGIC collaboration, set up by members of this RG with others – moving forward global analysis of germ cell tumour outcomes	Contributed data, contributed analysis
7. EORTC SPECTA-AYA: A unique molecular profiling platform for adolescents and young adults with cancer in Europe. de Rojas T, Kasper B, Van der Graaf W, Pfister SM,	This is the only European AYA-focused molecular profiling platform	The Subgroup initiated the study.

Bielle F, Ribalta T, Shenjere P, Preusser M, Fröhling S, Golfinopoulos V, Morfouace M, McCabe MG. Int J Cancer. 2020 Aug 15;147(4):1180-1184. doi: 10.1002/ijc.32651		
8. Taylor RM, **Fern LA**, Barber JA, Alvarez-Galvez J, **Feltbower R**, Lea S, Martins A, Morris S, Hooker L, **Gibson F**, Raine R, **Stark DP, Whelan JS**. (2020) Specialist age-appropriate care and quality of life outcomes in a longitudinal cohort of teenagers and young adults: the BRIGHTLIGHT study. BMJ Open e038471. doi:10.1136/bmjopen-2020-038471	BRIGHTLIGHT	Designed and implemented this programme of study. See also Koo MM, Lyratzopoulos G, Abel GA, **Taylor RM**, Barber J, **Gibson F, Whelan J, Fern LA.** (2020) Self-reported presenting symptoms and timeliness of help-seeking among adolescents and young adults with cancer: cross-sectional analysis of the BRIGHTLIGHT cohort. JAMA Open doi:10.1001/jamanetworkopen.2020.15437
9. Management of Late Relapses After Chemotherapy in Testicular Cancer: Optimal Outcomes with Dose-intense Salvage Chemotherapy and Surgery. **Alifrangis C**, Lucas O, Benafif S, Ansell W, Greenwood M, Smith S, Wilson P, Thomas B, Rudman S, **Mazhar D**, Berney D, **Shamash J**. Eur Urol Focus. 2020 May 4:S2405-4569(20)30099-7. doi: 10.1016/j.euf.2020.04.001.	Data pooling	Leading to biological examination of late relapses in Germ Cell Tumour Subgroup.
10. Adjuvant tyrosine kinase inhibitor therapy improves outcome for children and adolescents with acute lymphoblastic leukaemia who have an ABL-class fusion. Moorman AV, Schwab C, Winterman E, Hancock J, **Castleton A**, Cummins M, Gibson B, Goulden N, Kearns P, James B, Kirkwood AA, Lancaster D, Madi M, McMillan A, Motwani J, Norton A, O'Marcaigh A, Patrick K, Bhatnagar N, Qureshi A, Richardson D, Stokley S, Taylor G, **van Delft FW**, Moppett J, Harrison CJ, Samarasinghe S, Vora A. Br J Haematol. 2020 Dec;191(5):844-851. doi:	Scientific leadership	Informing collaboration on TYA ALL biology in next ALL trial

10.1111/bjh.17093. Epub 2020 Sep 14.		
11. High likelihood of actionable pathogenic variant detection in breast cancer genes in women with very early onset breast cancer. Evans DG, van Veen EM, Byers HJ, Evans SJ, Burghel GJ, **Woodward ER**, Harkness EF, Eccles DM, Greville-Haygate SL, Ellingford JM, Bowers NL, Pereira M, Wallace AJ, Howell SJ, Howell A, Lalloo F, Newman WG, Smith MJ. J Med Genet. 2021 Mar 23:jmedgenet-2020-107347.	Scientific collaboration	Contributing to germline predisposition study proposal
12. Lindner, O. C., Boon, I. S., **Joffe, J., & Stark, D**. (n.d.). Evaluation of the "Shared Community Follow-up" after a germ cell tumour—A novel initiative for remote cancer follow-up enhanced by online patient-reported outcome measures. European Journal of Cancer Care. doi:10.1111/ecc.13264	Initiated in Germ Cell Research Group many years ago	Basis of new follow-up study collaboration Quality of Life & Survivorship and Germ Cell Tumour Subgroup.
13. **BRIGHTLIGHT WORKSTREAM 1:** Lea S, **Gibson F, Taylor RM**. "Holistic Competence": How Is it Developed, Shared, and Shaped by Health Care Professionals Caring for Adolescents and Young Adults with Cancer? J Adolesc Young Adult Oncol. 2021 Mar 10. doi: 10.1089/jayao.2020.0120. Epub ahead of print. PMID: 33691496. **WORKSTREAM 2** **Primary outcome measure: quality of life** **Taylor RM, Fern LA**, Barber J, Alvarez-Galvez J, **Feltbower R**, Lea S., Martins A., Morris S., Hooker L., **Gibson F**., Raine R., **Stark D., Whelan J**., Longitudinal cohort study of the impact of specialist cancer services for teenagers and young adults on quality of life: outcomes from the	First systematic evaluation of TYA services, worldwide. Publication informed successful competitive funding of BRIGHTLIGHT_2021. We have published both primary and secondary outcomes and a patient and public involvement	Developed from feasibility study developed by Subgroup in 2009 and successful NIHR Programme Grant BRIGHTLIGHT. LF/RT are joint CI on new BRIGHTLIGHT_2021 study. Co-applicants from the Group and Subgroups include Dan Stark, Richard Feltbower and Martin McCabe

BRIGHTLIGHT study. BMJ Open 2020;10:e038471. doi: 10.1136/bmjopen-2020-038471 **Secondary outcome measure: Survival** **Fern LA, Taylor RM,** Barber J, Alvarez-Galvez J, **Feltbower R**, Lea S., Martins A., Morris S., Hooker L., **Gibson F**., Raine R., **Stark D., Whelan J**., Processes of care and survival associated with treatment in specialist teenage and young adult cancer centres: results from the BRIGHTLIGHT cohort study. BMJ Open 2021;0:e044854. doi:10.1136/ bmjopen-2020-044854 **Patient and public involvement** **Taylor, R.M**., Lobel, B., Thompson, K, Onashile A., Croasdale M., Hall N, Gibson F., Martins A., Wright D., **Morgan S., Whelan J,. Fern L.A.** BRIGHTLIGHT researchers as 'dramaturgs': creating There is a Light from complex research data. Res Involv Engagem 6, 48 (2020). https://doi.org/10.1186/s40900-020-00222-5		
END OF TREAMENT 14. Lea S, Martins A, **Fern LA,** Bassett M, Cable M, Doig G, **Morgan S, Soanes L,** Whelan M, **Taylor RM.** The support and information needs of adolescents and young adults with cancer when active treatment ends. BMC Cancer. 2020 Jul 28;20(1):697. doi: 10.1186/s12885-020-07197-2. PMID: 32723357; PMCID: PMC7388472.	Priority area of research for young people, identified by JLA and also the online needs study previously conducted.	Group members (RT, LF, LS, SM) submitted funding application to Teenage Cancer Trust (TCT), conducted study, published.
EARLY DIAGNOSIS 15. Forster A, Herbert A, Koo M., Taylor R., Gibson G., **Whelan J.,** Lyratzopoulos G., **Fern L.A**. Associations between diagnostic intervals	First publication, worldwide, demonstrating patient reported outcomes associated with diagnostic intervals	Developed from original Health Services Research working party strategy in November 2006.

with quality of life, clinical anxiety and depression in adolescents and young adults with cancer: the BRIGHTLIGHT cohort	and moves the attention away from shortening primary care intervals as a solution to improving outcomes for TYA.	
16. (2021) Surveillance for Subsequent Neoplasms of the Central Nervous System for Childhood, Adolescent and Young Adult Cancer Survivors: Recommendations from the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 22: e196-206. Bowers DC, Verbruggen LC, Kremer LCM, Hudson MM, Skinner R, Constine LS, Sabin N, Bhangoo R, Haupt R, **Hawkins MM**, Jenkinson H, Khan RB, Klimo Jr P, Pretorius P, Ng A, **Reulen RC**, Ronckers CM, Sadighi Z, Scheinemann K, Schouten van Meeteren N, Sugden E, Teepen JC, Ullrich NJ, Walter A, **Wallace WH**, Oeffinger KC, Armstrong GT, Van der Pal HJH, Mulder RL	International policy recommendations based upon review including TYACSS data	Developed within CSDG since 2006

Appendix 4

Recruitment to the NIHR portfolio

Summary of patient recruitment by Interventional/Non-interventional and number of studies opened/closed.

Year	All participants		Cancer patients only*		Number of studies	
	Non-interventional	Interventional	Non-interventional	Interventional	Opened	Closed
2016/17	758	142	758	142	2	2
2017/18	445	319	430	319	4	3
2018/19	811	422	801	422	1	4
2019/20	417	488	417	488	3	2
2020/21	456	446	456	446	2	0

The above table shows TYA and testicular cancer data.

*This data is based on a proxy from CPMS (the NIHR database used to collect patient recruitment data) and includes diagnostics, screening and prevention patients.

Appendix 5

Annual report feedback 2019-20

Areas of strength:

- The Panel commended the report submitted by the Group. They felt that the Group is very influential in the community and have really identified their niche in this research area and excel within it.
- The Panel thought that the way the Group approached their research and strategy in terms of starting with the understanding of what is needed for change in practice or policy and developing studies according to this is a credit to the Group. In line with this, the Group have clearly focused their strategy and objectives on the needs of the age group as opposed to being solely led by the scientific impetus.
- The Panel noted the significance and impact of the BRIGHTLIGHT study as well as the risk stratification tool the Group have produced.
- The Panel noted that the JLA study that the Group undertook was not mentioned in the achievements; this has been hugely useful to the community and informative to the field and is commendable. The challenge for the Group now will be to capitalise on this JLA study and get funders and collaborators to respond constructively.
- The Panel felt that the Group had clear collaborative working with several other Groups as well as good links with the NIHR, NHS, cancer charities and ECMC.
- The Panel highlighted the exemplary Consumer input from this Group as well as the clear excellent mentoring for Consumer members. The Panel were sorry to hear about Lara Veitch's passing and suggested that the NCRI communicate to the family that the report was dedicated to Lara and her invaluable input to the Group, if this was appropriate.

Areas which the Group need to consider:

- The Panel was concerned that the germ cell tumours portfolio seemed less developed and less strategic compared to the other areas in the portfolio. The Panel felt that the germ cell tumours arm of the Group had not yet found its niche and that the main Group could support them with this. More clarity is needed regarding the germ cell tumours strategy with clear outputs, exploring opportunities for innovation.
- Consumer involvement is a real strength of this Group. However, the Panel wanted to ensure that all the amazing work the Group requires consumer involvement for does not fall on one or two members. This Group is more adept than others, given their excellence with consumer involvement, to share insight with the NCRI and other Groups about how to reach out and utilise consumers. It was also noted that the Group may be able to suggest what the future of consumer involvement could look like. Are there any innovative ways in which we can have consumer input i.e. through technology, which would avoid taking people away from their jobs or studies too much?

Appendix 6

Quinquennial review feedback - 2021

Areas of strength:

- The panel highlighted that the Group demonstrated a strong legacy of research in GCT, that has been practice-changing, such as the 111 study. As for TYA, the very interesting observations from BRIGHTLIGHT specifically on shared care patients having worse outcomes and impressive work on social reintegration were noted to be extraordinary.

- The panel noted that the Group was well assembled and multi-disciplinary.

- The BRIGHLIGHT study is an internationally recognised study and is being watched by the entire community (internationally).

- The exemplary PPI activity was noted and was considered to be beneficial to both parties. There are a broad selection of projects, allowing the Group to bring more people in, including young people, and improve diversity.

- The panel noted that the Group is taking great strides in cancer care and members are very passionate about improving patient care.

- The panel highlighted that the Group has delivered significant work in HSR and LWBC research.

Areas of weakness:

- The panel discussed whether the merger of the GCT and TYA Group had been beneficial. It was suggested that the GCT Group lacks direction and cohesiveness and would benefit from a more diverse membership. The panel noted that the GCT Subgroup was lacking representation from population science, behavioural science and endocrinology.

- The panel felt the Group could be more intentional about the composition of members by disease Group and by profession. The panel recommended involvement of more trainees with the Group and its' activities.

- The panel was surprised to hear that age is not collected in the national data, which ideally needs to be resolved. The panel questioned if there was any other way of obtaining this data outside of waiting for the National Institute of Health Research (NIHR) to make the appropriate changes.

- The panel encouraged the Group to decide specific actions that could be taken to aid the Biobanking issue. It is important that the Group work with other stakeholders to improve this and to develop a cohesive strategy for sample collection.

- The Group is lacking disease-specific representatives which could aid identification of clinical and biological issues that relate to different diseases.

- A lot of work that the Group has developed has unfortunately not been funded and the Group should try to identify funding streams outside of CRUK, which appears to be quite heavily relied upon.

- While the Group was commended on its' health service research and survivorship research the panel encouraged the Group to focus more on clinical, translational and

biological issues. The Group could also benefit from having a strategy for the subset of patients who do poorly/recurrent or relapsed patients.

- The Panel encourage the development of stronger links with industry to aid prioritisation and new treatments and new drug developments.

- The Group should think about how they can link up more internationally to develop trials and research.

Issues for the NCRI to consider:

- To work with the TYA and GCT Group to understand how the merger has affected the GCT subgroup and work to ensure that the GCT subgroup continues with a good sense of direction and key priorities.

- The NCRI should consider supporting the recruitment of more consumers for the Group as well as diversifying the recruitment process, as appropriate.

- The NCRI should consider how LWBC research can be combined, perhaps with the Children's Group or with the LWBC Group.

- The NCRI should facilitate the recruitment of a wider range of expertise and disease-specific representatives onto the Group.

- The NCRI should support the Group, through a strategy day, the identification of more clinical, biological and translational research questions.

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