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NCRI Teenage and Young Adults & Germ Cell Tumour Group

Annual Report 2018-19

Partners in cancer research

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1. Top 3 achievements in the reporting year

Achievement 1 The publication in Lancet Oncology in 2019 of the second malignant neoplasms data and analysis from the UK TYA cancer survivorship cohort study. This study was developed and implemented within the Teenage and Young Adults & Germ Cell Tumour CSG (TYA & GCT). The paper complements our previous publications on cardiac outcomes. The editorial accompanying the article emphasised the novel fundamental reconsideration emerging from this data, of the aetiology and nature of second malignant neoplasms after TYA cancer, towards lifestyle causes and somewhat away from iatrogenic causes that are prominent in younger children. This large cohort is now developing enhanced clinical data, patient reported outcomes data and wider data linkage, and developing its role as the basis for intervention studies in lifestyle.
Achievement 2 Specific targeted collaborations are in place between our TYA & GCT CSG and other clinical studies groups including in radiotherapy, pharmacology and Living with and Beyond Cancer. This has been an objective of the CSG for some years, and we have built upon that work in this reporting year to deliver this. The James Lind Alliance priorities and our more recent links to other site specific CSGs that involve TYA patients will assist further. Now we have to create funded studies from these collaborations using the James Lind Alliance research priorities, and detailed discussions of that are featuring in upcoming multi-centre grant applications.
Achievement 3 The formation of the Germ Cell Tumours Subgroup was a final substantial goal in the merger of the TYA and the GCT CSGs, which is now complete. Over and above that, the Subgroup has already been successful, with the integration of it work within leading international collaborations and a healthy portfolio of open and developing trials and studies. Obtaining the support of the MAGIC group for a carboplatin strategy in all advanced seminoma and extra-cranial dysgerminoma (Shamash) has led to the formation of an international study development group. The Subgroup had its first meeting in Q1 2019, including planning studies

correlating acute with long term toxicities during combination chemotherapy, the psychological impact of orchidectomy patients <16 years, and outcomes from minimally invasive retroperitoneal surgery in men.

2. Structure of the Group

The CSG continues to function through our 4 subgroups: Health Services Research (HSR), Biological Studies, Survivorship and Germ Cell Tumour.

The formation of the GCT subgroup responds to the needs of the research community after our merger. Gynaecological germ cell tumours now feature within the germ cell subgroup and portfolio trials. Joint part-meetings between the Children's Cancer & Leukaemia CSG Germ Cell Tumour Subgroup and the TYA & GCT Germ Cell Tumour Subgroup will be explored in the upcoming 12 months.

The new agenda for the clinical studies group meeting has been implemented, hearing presentations of new and updated research proposals that relate to TYA and/or germ cell tumours, advising and problem-solving from them, building collaborations, generating new ideas, drawing the group and subgroups together and involving much less process & updating of routine ongoing actions. This responds in part to the 25th September letter to us from the NCRI. We expect to engage a wider of range of the research community in this manner and encourage more research to become included appropriately in the TYA & GCT trial portfolio. Our grant applications this year also indicate this widening of our engagement and impact.

With its current membership and relationships, the group has delivered considerable influence upon the NHS processes that can influence research delivery. Stark working with Fern, McCabe (also NCRAS), Soanes, Feltbower and others have used their influence from the NCRI group, and our research, to ensure that substantial elements of the NHS England current draft service specification contain considerable elements that relate to research. These include; metrics and pathways, the storage of tumour tissue and the mandating the discussion of research participation from the NCRI portfolio where there is a trial open, even if only at another hospital location.

In this reporting period we have seen some change in our membership. Some members have left or changed roles and we are very grateful for their work.

Angela Jesudason and Jonathan Shamash complete their term as Co-Chairs in May 2018. Dr Shamash remains a member of the group in his role as chair of the GCT Subgroup. Danish Mazhar and Hamish Wallace who have both rotated off the CSG and joined the Survivorship Subgroup. Linda Evans, Lisa McCann, Maria Michelagnoli, Shaun Wilson, Benjamin Thomas, James Adams, Veronica Moroz, Johnathon Joffe have also rotated off the CSG.

Our previous trainee members Chris Barton, Okezie Ofor, Peter Hall, and Rebecca Ling have now completed their term as trainees,

Further information on our new members and their responsibilities are listed in Appendix 1.

3. TYA & GCT Group and Subgroup strategies

Our overarching *purpose* as a CSG is appended and remains unchanged from 2017-18. Within our specific projects to deliver this, within this reporting period, we are very largely delivering on time according to our 2018-19 strategy. Within our strategy as a group, both main and subgroups, 26 milestones or outputs required action between May 2018 and May 2019. Fourteen of those are completed, 8 of them are on track for completion but not yet completed, and 4 are delayed. Each of these 4 objectives have specific measures in place to complete it.

Below is our current prioritisation of our aims within those published in July and August 2018 (appended). Note that several key 18-19 aims are already achieved as above, including the Germ Cell Tumour Subgroup, TYA leads for site-specific CSGs and evolving the main group meeting. Several are now joint aims across the main and subgroups, as the work has evolved and may be listed in one suitable place, e.g. consumer engagement, JLA question in a site-specific trial.

TYA & GCT Group

National prospective Reproductive function study, in young adult cancer patients across the UK.

This is a joint objective between the CSG and the Survivorship Subgroup

This proposal will:

- Generate large-scale data on pre- and post-treatment reproductive function, based on biomarkers, to allow the development of prediction tools for long-term fertility and reproductive lifespan
- Collect pre- and post-treatment biological samples for the assessment of reproductive function
- Establish assessment of post-treatment reproductive function as a routine part of long-term care for UK TYA cancer patients.
- Develop and pilot a patient decision aid to support male and female TYAs specifically to make fertility preservation treatment decisions.

This would be a huge national and international first and will generate a large impact for the CSG. This project will be subject to funding application by the end of Q1 2020.

Understanding TYA Radiotherapy outcomes

Developing specific collaborative research proposals with the radiotherapy research community. We have built the collaboration and achieved workshop funding with CTRad to develop the proposals in June 2019. We have developed TYA-specific epidemiological outcomes analyses proposals as well, for funding application in May 2019. There may well be biology and health services questions to build in cross-subgroup working also, so this is a joint objective with those subgroups.

Developing further research into the clinical pharmacology of TYA with cancer

The CSG and Biological Studies Subgroup are actively collaborating in the research opportunities arising out of changes in the age-related availability of clinical trials, as going forward through the FAIR trials group, which is aiming to lower the age of eligibility for Drug

Development Trials to 13 years. Dan Stark has met with the north of England collaboration of adult ECMCs, who are interested to collaborate with us on this project and discussed with the Biology Subgroup, and with the leads for the Accelerate program. A wider national meeting will take place before Q4 2019. This may also improve the availability of trials to TYA, relevant to aim 6 below.

Assess, influence and re-assess our impact as a CSG upon our clinical and research community.

Hadeel Hasan has been invited to create public and healthcare professional digests of our CSG's activity suitable for social media and newsletters for example.
The CSG has prepared a survey testing the awareness in our TYA and GCT communities of the work of the CSG. This will be followed by sharing digests, and we will then re-run the survey around 12 months later to re-assess our impact. This is partly in response to the letter to us from the NCRI of September 2018, to engage the wider TYA community and extend the reach of work that is included in the NCRI portfolio.

The refresh of the NCRN/NIHR strategy for TYA with cancer in April 2019, led by Burke as a collaborative exercise with the NCRI and NHS England as partners, prioritised several future areas of CSG work that will enter our strategy once refined.

We are contributing to the CRUK National Chemotherapy Board Steering group developing TYA-specific regimen consent forms - Shamash with Mansi, Nicholson, Hobin and others. This will open up research opportunities for decisions research and for applied research in medical communication. Preliminary discussions with researchers with these areas of expertise have been undertaken recently

Making better use of the NCRI portfolio

We are working in detail with the NIHR, the NCRN cancer cluster and CRUK upon the nature of the portfolio map for the TYA & GCT CSG. When optimised, this map can inform the clinical community, support trial recruitment data in real time, and help us to increase trial participation using the included trials and the design of the web space. This project is early in development.

Trial participation in TYA as an applied health research project

This is a joint objective with the HSR Subgroup, to evaluate the impact of a change in TYA research structures.
Fern, Feltbower, McCabe and Stark have initiated a research collaboration between this NCRI group, NHS England/Improvement (Hough) and the NIHR cancer cluster and National Cancer Research Network (Burke). The CSG is leading, developing a programme of research that gains specific and transferrable learning from the shifts in the TYA clinical trial recruitment environment as a result of the specific NIHR, NCRI and NHS England changes between 2020 and 2025, resulting from the Cancer Strategy 2015. The implementation of those changes, their influence upon the barriers and facilitators of recruitment (in our previous work as a CSG 'the "5As') and the research culture in TYA cancer departments will result in variation in recruitment patterns over time and geography. Specific study objectives have been shared, the core team has met on 3 occasions and the membership, collaborations and design are being developed for national grant funding by Q1 2020. Intervention studies about the offer of

research in general and using digital approaches to support the explanation of research to TYA are also in detailed discussion in this group.

Our CSG as a whole also has several very new projects, just in germination, which we should advance over the next 24 months

1. Palliative care for TYA - Darlington from the HSR subgroup is an active participant and grant holder of the global accord grant, studying palliative care professional training needs of TYA healthcare professionals, and leading to intervention study. This would be an area for future collaborative work for the CSG, nationally and internationally
2. Joint work has been informally discussed with the Psychosocial Oncology CSG and survivorship group, about PRO measures for caregivers in TYA
3. There is a national Premature Ovarian Failure intervention trial due to open soon that is not currently on the NCRI TYAG portfolio, despite being a key issue for young women and women with germ cell tumours.
4. TYA & GCT CSG has begun work with the NIHR Nutrition and Cancer initiative. Two CSG members are active in the NIHR Nutrition and Cancer young people's track. Studies here should feature in the NCRI portfolio.

Biological Studies Subgroup (outgoing Chair, Dr Martin McCabe)

Of our strategic aims in the 2017-18 report, 2 of 3 are delivered.

From a successful pilot, plan personalised medicine intervention studies in TYA During the last year, SPECTA-AYA has opened and is recruiting AYA patients aged 12-29 with high grade gliomas and intermediate and high grade sarcomas. This is a collaboration between NCRI, EORTC, the International BioBank of Luxembourg and the German Cancer Research Centre, Heidelberg. Two international central pathology review panels have been developed for gliomas and sarcomas respectively. A monthly international molecular tumour board has been convened. A preview paper will be submitted to Eur J Cancer in Q2 2019 to publicise the study. We aim to build from this pilot towards funding (possibly from EORTC again) for a molecularly driven trial (anticipate output date May 2021), either a basket or disease-specific design.
Dose intensity registry and pooled trial data analysis funded Application to the NIHR for a doctorate training fellowship was delayed by maternity leave and is planned for June 2019. The objectives remain unchanged.
To address the low levels of TYA tissue banking via the CCLG tissue bank There has been further discussion within the CCLG tissue bank steering group to progress this complex aim. The facilitators and barriers tissue banking as routine NHS TYA cancer care has not progressed due to staffing changes. Specific actions are planned:

- Communication to existing CCLG tissue bank sites with co-located adult units to promote tissue banking to TYA patients. Complete an evaluation in 2019 to understand the variation in TYA samples from these centres.
- A discussion document will be prepared before the end of Q3 2019 to plan further work with CM-Path.
- Alignment with a specific research project that involved tissue banking as a core component. See new strategic aim 6 below.

We were disappointed this year that the implementation of Whole Genome Sequencing within the NHS did not extend its age beyond 19th birthday, despite the rationale for younger children applying equally to TYA. We were encouraged that work to increase the availability of tissue specimens was included strongly in the NHS England draft service specification for TYA with cancer. Next year we aim to work with the NHS England Clinical Reference Group to lobby for this to change.

Radiobiology, pharmacology, and age

Joint with the CSG – see their aims 2, and 3

Appoint a new subgroup chair

Sarah Pratap joined the group and has agreed to chair the Biological Studies Subgroup.

Genomic medicine studies

Two new members were appointed to the Biological Studies Subgroup in March: Dr Sam Behjati, an academic paediatric oncologist with expertise in genomic profiling, and Dr Emma Woodward, a clinical geneticist with expertise in cancer predisposition. The group agreed to scope two parallel projects:

i An evaluation of an existing large, collaborative WGS dataset collated from Heidelberg, St Jude's, the Broad and Sanger Institutes to examine the prevalence of pathogenic germline mutations in AYA patients, and age-related variation in known pathogenic somatic mutations

ii A prospective UK study of pathogenic germline cancer predisposition mutations, either pan-cancer or in defined subsets. We aim to make project the focus of strategic aim 3 to motivate increasing banked tissue across TYA.

The Subgroup sees potential for collaborative work with the HSR subgroup for this project.

Germ Cell Tumour Subgroup (Chair, Dr Jonathan Shamash)

Implementation of micro-RNA into germ cell tumour management Matthew Murray is developing a proposal for NHS implementation. Existing grants such as AGCT 1531, P3BEP and developing projects such as carboplatin in Seminoma/Dysgerminoma are already contributing substantially to this aim, as is PPI work, below. This is a longer term aim, but we plan to have a proposal in May 2020 to discuss with the NHS England clinical reference group.
Patient and Public Engagement Improved This is a joint aim with the HSR subgroup and main CSG, to encourage consumers to co-ordinate more, and refresh that aspect, as per the NCRI letter to us of September 2018. To ensure the sustainability of patient and public engagement work, in GCT. We have been addressing this by working on virtual PPI groups, in the context of the CRUK pilot virtual network for children's PPI. In March 2019 a GCT consumer group workshop facilitated was held by Matthew Murray, Lorna Fern and Nicola Pettitt. Recruitment was with assistance from the alliance of smaller GCT charities. This workshop focussed upon the place of MiRNA in clinical management of germ cell tumours and second workshop is planned for late June. This enhances, not replaces, consumers on the NCRI group and subgroups, by providing a specific sounding board for our committed GCT consumer representatives. A lead for this initiative is still to be confirmed.
Age and GCT outcomes Richard Feltbower will lead this in collaboration with NCRAS as a registry-based study. We have built detailed discussion into the CSG meeting in April 2019 and invited Glaser to attend to contribute PRO methods and will therefore achieve our planned milestone.
Stratified treatment in resistant disease The grant by Protheroe et al submitted in this reporting period is the milestone for this objective and will deliver this if funded.
Studies to reduce toxicity and maintain efficacy Opening the AGCT 1531 study in the UK by Q3 2019 will address this in part. The Shamash design for carboplatin in seminoma will be developed by the international trial development group and contribute to this aim. A project in early development, accelerating treatment in good prognosis GCT to avoid the need for bleomycin, can contribute to this aim.
Extend the evaluation of CXC-12 as a prognostic and predictive biomarker in non-seminomatous GCTs This project, arising an ICR germ cell biology project, is awaiting final confirmation as a translational sub-study in the AGCT 1531 trial.

Survivorship Subgroup (Chair, Professor Michael Hawkins)

The Survivorship Subgroup met on Wednesday 7th November 2018 and will meet again in June 2019. During the reporting year members of the Survivorship Subgroup have submitted two applications to Children with Cancer UK. One entitled "Establish a comprehensive surveillance system for adverse health outcomes in British survivors of childhood, teenage and young adult cancer", £350k over 3 years, PI Prof Hawkins. The other entitled "Pilot study to investigate self-reported health behaviours in survivors of teenage and young adult cancer", £50k over 18 months, PI Dr Raoul Reulen.

New TYA Cancer Survivor Studies (TYACSS) linkages

In March 2019 Prof Hawkins was awarded a new grant to begin October 2019 entitled "Establishment of national system to monitor the risks of adverse health outcomes among the entire population of survivors of childhood, teenage and young adult brain tumour in Britain"; £300,000 for 3 years, PI Prof Hawkins, funded by The Brain Tumour Charity.

As part of an existing grant with Children with Cancer UK, 2017-2020, entitled "Risk stratification of the national population of survivors of childhood, teenage and young adult cancer for evidence-based clinical follow-up"; £250,000, PI Prof Hawkins, we produced a landmark publication on the risk of subsequent primary cancer in survivors of teenage and young adult cancer Lancet Oncol (2019) 20:531-545, the accompanying editorial pages 466-467, indicates the substantial contribution made.

A new PhD student starts with Prof Hawkins in October 2019 funded by a grant awarded by Public Health England (PHE) in 2018 to analyse the national PHE database of GP prescriptions. The PhD is entitled: "Long-term morbidities managed in primary care among survivors of childhood, teenage and young adult cancer". This is the first time cancer survivors have been linked to GP prescriptions at a national level.

Plan germ cell LE analyses

We initially plan a publication which investigates pregnancy and labour complications in female survivors of teenage and young adult cancer using the TYACSS cohort. We previously published on such outcomes within the British Childhood Cancer Survivor Study (Reulen R et al (2017) Pregnancy and Labor Complications in female survivors of childhood cancer: The British Childhood Cancer Survivor Study. J. Natl Cancer Inst 109(11):djx056 doi:10.1093/jnci/djx056).

In the TYACSS cohort there are 24,309 and 4885 5-year survivors of testicular and ovarian cancers, respectively.

Develop new models of follow up evaluation or trial

Work with Danish Mazhar to develop his proposed study of remote follow-up of survivors of testis cancer – in terms of benefits to patients with respect to psychological morbidity, anxiety, quality of life and economic costs.

Cerebrovascular Case-control study

Using the TYACSS cohort we published (Circulation (2017) Chloe Bright et al. "Risk of cerebrovascular events in 178962 5-year survivors of cancer diagnosed at 15 to 39 years of age"; 135:1194-1210) a manuscript that reported that by 60 years of age 9%, 6% and 5% of CNS tumour, head and neck cancer and leukaemia, respectively, have been hospitalised for a cerebrovascular event, where as 2% would have been expected from rates in the general population.

Submitted for publication is a comparable publication relating to survivors of childhood cancer which revealed that by 65 years of age 26% of survivors of a childhood brain tumour treated with cranial irradiation have been hospitalised with a cerebrovascular event when 4% would be expected from rates in the general population.

We are planning a case-control study of such cerebrovascular events to determine the role of the following factors in the development of the events:

- Cumulative exposure to radiation of cerebral vasculature and cumulative exposure to individual cytotoxic drugs
- Survivor questionnaires – ethnicity, hypertension diabetes, history of cardiac problems, dyslipidaemia stress, depression, smoking, alcohol, waist-to-hip ratio, diet, physical activity.
- Genotypic factors from DNA extracted from saliva

Health Services Research Subgroup (Chair, Dr Lorna Fern)

The subgroup has had another successful year with a record number of funding submissions, nine applications have been submitted and so far, three have been successful with the outcome not know on two. We have also brought onto the Group Professor Sam Ahmedzai to develop our new End of Life Workstream along with Anne-Sophie Darlington. This is a new Group in response to the end of life research questions which are in the JLA Top 10 priorities, it has met once so far by teleconference and are still formalising their priorities. Consumer members Max Williamson and Lara Veitch continue to be instrumental to our work.

Ongoing evaluation of NHS services for TYA with cancer

To continue to create impact and future research from the BRIGHTLIGHT cohort

After the £2m programme grant was funded to December 2017, the study was awarded a no cost extension until May 2018, and since Whelan, Taylor & Fern were awarded a further costed extension until December 2019 with £150k to complete analysis and dissemination year. Three papers have emerged from the study this year, the first paper for the Cohort has been accepted in the BMJ open and describes demographics, baseline characteristics, we also published ten years of patient and public involvement and conceptualising age-appropriate care from Workstream 1. A number of papers are being prepared. The whole research team including subgroup members Fern, Taylor and Stark are meeting monthly with the statistician to interpret the results. The March 1st conference was cancelled due to small numbers. We

aim to disseminate the BRIGHTLIGHT results to the UK at this year's TYAC conference in November 2019.

We are committed to continue the work of BRIGHTLIGHT and pursue following on funding this. Taylor applied for a fellowship, which was successful at stage 1 and did not progress following Stage 2.

We completed the 'End of Treatment' needs study and have successfully secured funding for a cancer alliance fellowship to develop interventions based on results.

The impact of TYA age on pathways to diagnosis

We have continued with our collaboration with UCL. The symptom manuscript will be submitted later this year and has been slightly delayed due to the complexity of the data and also staff change over. The data has been presented extensively orally at international and national conferences. Dr Fern was successful in a competitive bid to Sarcoma UK for secondary data analysis of the SAM study data. 'The diagnostic experience of sarcoma patients; secondary analysis of the SAM study (development of a sarcoma-specific patient-reported outcome measure) £24,000K' the Group also have a tentative submission for 'Clinical and Patient Reported Outcomes associated with pre-diagnostic intervals for teenagers and young adults with cancer: secondary data analysis of the BRIGHLIGHT Cohort £70,000'

Use the JLA to influence funding

Group members have been involved in extensive dissemination through multiple channels including newsletters, conference presentations, invited meeting presentations, funders and CSGs. We have met with funders Cancer Research UK, Kids and Teens and NIHR. Some of the key TYA questions are 'out of remit' for CRUK and our questions have to undergo a further selection panel for NIHR before a themed call is considered. These conversations are continuing.

We have developed links with the NCRI Living With and Beyond Cancer PSP and identified areas for collaboration between the two PSPs. Subgroup member Sam Ahmedzai presented the TYA PSP alongside the LWBC PSP at the NCRI meeting day in Manchester. Bringing together funders, CSGs, researchers and cancer alliance representatives. Following on from the meeting in March we hope to be able to bring keep collaborators together to codevelop studies.

We have created a group within the Subgroup lead by Sam Ahmedzai and Anne-Sophie Darlington to develop studies around end of life care. This was a priority area identified by the JLA and we did not have this in the current portfolio. The Group has national representation including Scotland and Wales. Stark, Fern and Jesudason, spoke at the CCLG/TYAC strategy day, with the potential for pilot-grant funding for TYA James Lind Alliance priorities, but the challenge of that inhibiting larger NCRI group funders.

4. Task groups/Working parties

Remit of Early Onset Carcinoma Working Party
To identify and characterise the clinical features of carcinomas developing aged under 40 in the UK. To develop collaborations between the TYA and site-specific CSGs. 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
Progress to date
Cross cutting group established, with membership from Breast, Gynaecological and Colorectal Groups. Draft proposal has been prepared. The first phase of the project is to interrogate the cancer registry for baseline epidemiological information, available treatment and outcomes for women <40 years and compare them with women 40+years with focus on breast colorectal and ovarian carcincoma and all other cancers combined. Application for Open Data release is in preparation with support from colleagues from the Office for Data Release, PHE. This will inform and support application for funding.

5. Funding applications in last year

The multicentre psychological distress application by Stark and Fern with others reported in 2018 was unsuccessful but detailed feedback and a specific invitation to resubmit was received and resubmission is planned for 2019

The social integration application by Stark and others reported in 2018, to ESRC, is under discussion at the March 2019 panel, almost one year after submission, with no outcome known to us.

Table 2 Funding submissions in the reporting year

Cancer Research UK Clinical Research Committee (CRUK CRC)					
Study	**Application type**	**CI**	**Outcome**	**Level of CSG input**	**Funding amount**
November 2018					
TARSAN - A trial to assess doxorubicin and dasatinib treatment in patients with refractory p53 wild type testicular germ cell tumours carrying a homozygous KIT ligand (KITLG) single nucleotide polymorphism (SNP).	CTAAC outline application	Andrew Protheroe	Pending	PI is CSG member. Presented for peer review	~£1.4 million
rEECur: International Randomised Controlled Trial of Chemotherapy for the Treatment of Recurrent and Primary Refractory Ewing Sarcoma	CTA full application	Martin McCabe	Pending	PI is CSG member. Presented for peer review	£1,710,403.73
Other committees					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of CSG input**	**Funding amount**
A multicentre feasibility study of prehabilitation and restorative rehabilitation during the treatment pathway of adolescents and young	NIHR ICA CDF for submission 30th April 2019	Dr. Matthew Maddocks	Pending	Member submitting	TBC

adults (15-39) years old undergoing allogeneic haemopoietic stem cell transplant					
End of Life Care for Babies, Children and Young People	NIHR HTA	LK Fraser	Pending	CSG consulted (Feltbower, Co-I)	£1.1M
Investigating educational outcomes in children and teenagers diagnosed with cancer	ESRC SADI	RG Feltbower	Unsuccessful	No input	£300,000
Evaluating the side effects and late consequences of treatment using novel primary and secondary care data linkage and population-based specialist Children's and TYA cancer registration data	CCLG Little Princess Trust Project Grant	RG Feltbower	Unsuccessful	No input	£120,000
Understanding and measuring the impact of brain tumours in children and young adults on quality of life	Brain Tumour Charity	RG Feltbower	Unsuccessful	No input	£300,000
Investigating education outcomes in children diagnosed with cancer	Candlelighters Trust	RG Feltbower	Unsuccessful	No input	£182,000
ARTISTIX. A randomised trial of intravenous steroid therapy +/- infliximab for gastrointestinal side effects in cancer immune checkpoint therapy.	NIHR HTA	Matthew Wheater/ Gareth Griffiths	Unsuccessful, but resubmission invited for 2019	Specific peer review about TYA issues	Approx. value: £2m (over 6 years)

EORTC 1553 SPECTA: RP1759 AYA pilot	Funding leveraged from EORTC to support this pilot	Martin McCabe	Funding agreed	Members devised the idea, developed and leads the protocol	Equivalent to ~€400,000
Establishment of a national system to monitor the risks of adverse health outcomes among the entire population of survivors of childhood, teenage and young adult brain tumour in Britain	The Brain Tumour Charity	MM Hawkins	Successful	PI is CSG member	£300,000
Colorectal adenoma and cancer after treatment for pediatric cancer – risk, risk factors and surveillance guidelines	The Dutch Cancer Society	Dr Raoul Reulen	Successful	PI is Survivorship Subgroup Member	€81,000
Establish a comprehensive surveillance system for adverse health outcomes in British survivors of childhood, teenage and young adult cancer	Children with Cancer UK	MM Hawkins	Pending	PI is CSG member	£350,000
Pilot study to investigate self-reported health behaviours in survivors of teenage and young adult cancer	Children with Cancer UK	Dr Raoul Reulen	Pending	PI is Survivorship Subgroup Member	£50,000

A multicentre feasibility study of prehabilitation and restorative rehabilitation during the treatment pathway of adolescents and young adults (15-39) years old undergoing allogeneic haemopoietic stem cell transplant	NIHR ICA CDF for submission 30th April 2019	Dr. Matthew Maddocks	Pending	Member submitting	TBC
An evaluation of the delivery of clinical trials to teenagers and young adults with cancer	Welcome Trust Research on Research	Rachel Taylor/Lorna Fern	Not invited to second round	HSR subgroup led	£ 176,371
Research Nurses Investment and partnership with NIHR	Teenage Cancer Trust	Rachel Taylor/ Lorna Fern	Rejected	HSR Subgroup led	£100,000
The diagnostic experience of sarcoma patients; secondary analysis of the SAM study (DEVELOPMENT OF A SARCOMA-SPECIFIC PATIENT-REPORTED OUTCOME MEASURE: SUK102.2016)	Sarcoma UK	Lorna Fern	Successful	HSR Subgroup led	£24,000
Clinical and Patient Reported Outcomes associated with pre-diagnostic intervals for teenagers and young adults with cancer: secondary	Cancer Research UK	Lorna Fern	Full application invited	HSR Subgroup led	£70,000

data analysis of the BRIGHLIGHT Cohort					
Do specialist Services for young people with cancer add value: BRIGHTLIGHT (Extension)	NIHR	Jeremy Whelan (Fern/Taylor)	Successful	Project originating from HSR Subgroup	£150,000
Improving quality of care and quality of life for teenagers and young adults living with and beyond cancer: the BRIGHTLIGHT extension study -	NIHR	Rachel Taylor	Not progressed after stage 2	Project originating from BRIGHTLIGHT	£903,224
Improving clinical assessment of treatment-related sexual morbidity in young people with cancer: young people and health professional perspectives	General Nursing Council Trust	Louise Soanes	Pending	Project arising from BRIGHTLIGHT PPI and led by HSR subgroup members Soanes/Fern Six consumer collaborators	£40,000
How can an online peer to peer information system be used effectively to improve information provision for teenagers and young adults with cancer	Macmillan	Lorna Fern	Not invited to second round	Project arising from previous online study by subgroup. All members including our consumers	£152,377
Developing an intervention to support teenagers and young adults at the end of treatment	Cancer Alliance	Louise Soanes	Successful	Project arising from previous End of Treatment study by subgroup.	One year fellowship funding https://rmpartners.nhs.uk/wp-content/uploads/2019/

					03/Pan-London-Research-Fellowships-project-info.pdf

6. Consumer involvement

Lara Veitch

The consumers continue to be instrumental to the work of the CSG and Subgroups. Lara is a member of the JLA team and has been involved in dissemination, as co-authors on the main manuscript and delivering oral presentations along with the other young people on the JLA project.

Max Williamson

Max has been heavily involved in the TYA Cancer community over the last year, with consumer work both within and outside of the NCRI CSG. Within the CSG, Max has regularly contributed to the work of the CSG as a consumer representative for the Health Services Research and Survivorship Subgroups. He has been listed as a co-author on the BMJ Open submission for the James Lind Alliance TYA Priority Setting Partnership (PSP). He has presented the work of the JLA project and the consumer involvement work of the TYA/ Germ Cell Tumour CSG at national (TYAC Conference, September 2018) and international (EuHIC, May 2018) research conferences. A co-presentation of the JLA PSP results with Professor Faith Gibson at the TYAC conference earned them the conference's Lisa Thaxter Award for best verbal abstract. Max also presented on the importance of consumer involvement in defining the TYA cancer strategy at the recent NIHR TYA CRN Summit in March 2019. Max currently sits on two TMGs (TIGER and UK P3BEP) within the CSG's research portfolio. He was also involved in the application of the TARSAN trial, writing a letter of support on behest of the TMG. As a Germ Cell Tumour Patient, he was listed as a co-author for the review "AYA Testis Cancer: the unmet challenge" (Paed. Blood & Cancer, 2019) with CSG members Dr Sara Stoneham, Dr Matthew Murray and Dr Benjamin Thomas.

Max is also a patient representative for the CCLG MaGIC Germ Cell Tumour Conference Organising Committee. Outside of the CSG, Max continues various consumer involvement projects including presentations for the NCRI Consumer Forum, written work for the ACCELARATE FAIR trials working group, and involvement with the MRC CTU at UCL PPI group and as a patient representative for a CCLG-funded systematic review into surveillance imaging in childhood cancer. Max has renewed his consumer membership within the CSG for another rotation until December 2022. He would like to thank Dr Lorna Fern for her continued guidance as a mentor, and the CSG and NCRI Consumer Forum in their relentless support.

7. Priorities and challenges for the forthcoming year

Priority 1 Obtaining funding for a national multicentre study of fertility biology during and after cancer treatment in TYA. The project is being led by Professor Hamish Wallace from Edinburgh, within the Survivorship Subgroup. The proposal is complete and has been presented and is supported by the CSG.
Priority 2 To resubmit our programmatic application for intervention in psychological distress in TYA with cancer. Includes a multicentre randomised controlled trial.
Priority 3 To open the multicentre MAGIC AGCT 1531 clinical trial for GCTs across the TYA community in the UK.
Challenge 1 A list of TYA leads for key site specific clinical studies groups have been identified for all relevant CSGs except lymphoma. We are very grateful to Nicola Keat and colleagues for undertaking this work. The challenge now is to put processes in place where the pipeline of studies and development from those CSGs is made known to the TYA & GCT CSG early enough to embed TYA specific sub studies in those evolving trials. We will identify areas from this to address the James Lind Alliance TYA specific research priority questions, and a collaborative approach to funding.
Challenge 2 Widening the capacity within the CSG to deliver our research. Our plan with the NCRI for natural attrition after the merger is achieved. Now we are beginning to lack capacity to deliver the research. The group benefits greatly from the work of the research and development co-ordinator Lorna Fern, an internationally respected researcher in her own right. However, the volume of grant development, patient and public engagement in current and planned projects and writing is growing beyond this capacity now. Building upon our strengths noted in the 2017-2018 Annual Report feedback letter, we're progressing our international leadership as a CSG including the global accord, SIOP Europe, and ESMO. None of these have research funding channels at present, but they are key to impact and collaboration.
Challenge 3 Intervention trials

We have a challenge recruiting involvement actively from a cancer-prioritising Clinical Trials & Research Unit. Fewer are interested in the complex interventions which are increasingly prevalent in TYA research, and many lack the capacity for work in this area.

8. Collaborative partnership studies with industry

Alphabot is a National machine learning small enterprise. They have agreed to work with us in developing chatbot technology, which has the potential improve the quality and understanding of patient consent to clinical trials.

9. Appendices

Appendix 1 - Membership of the TYA & GCT Group and subgroups

Appendix 2 – TYA & GCT Group and Subgroup strategies

A – Main CSG Strategy
B – Biological Studies Subgroup Strategy
C – Germ Cell Tumour Subgroup Strategy
D – Health Service Research Subgroup Strategy
E – Quality of Life & Survivorship Subgroup Strategy

Appendix 3 - Portfolio Maps

Appendix 4 – Top 5 publications in reporting year

Appendix 5 – Recruitment to the NIHR portfolio in the reporting year

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Dr Dan Stark (Teenage & Young Adults (TYA) and Germ Cell Tumour (GCT) Group Chair)

Appendix 1

Membership of the Teenage & Young Adults (TYA) and Germ Cell Tumour (GCT) Group

Name	Specialism	Location
Dr David Cutter	Clinical Oncologist	Oxford
Dr Hadeel Hassan*	Clinical Research Fellow	Leeds
Mr Stephen Francis Thomas	Consumer	Cardiff
Miss Lara Veitch	Consumer	London
Mr Max Williamson	Consumer	Bedford
Mr Vincent Wolverson	Consumer	Norwich
Dr Richard Feltbower	Epidemiologist	Leeds
Professor Mike Hawkins	Epidemiologist	Birmingham
Dr Ben Carpenter	Haematologist	London
Dr Anna Castleton	Haematologist	Manchester
Dr Andrew Protheroe	Medical Oncologist	Oxford
Dr Alison Reid	Medical Oncologist	Surrey
Dr Naveed Sarwar	Medical Oncologist	London
Dr Jonathan Shamash	Medical Oncologist	London
Dr Dan Stark (Chair)	Medical Oncologist	Leeds
Ms Bethan Ingram	Nurse	Cardiff
Mrs Nicola Pettitt*	Nurse	Birmingham
Dr Louise Soanes	Nurse	Birmingham
Dr Julia Chisholm	Paediatric Oncologist	London
Dr Angela Jesudason	Paediatric Oncologist	Edinburgh
Dr Martin McCabe	Paediatric Oncologist	Manchester
Dr Matthew Murray	Paediatric Oncologist and Translational Scientist	Cambridge
Dr Sara Stoneham	Paediatric Oncologist	London
Dr Clare Verrill	Pathologist	Oxford
Mrs Carla Reid	Physiotherapist	London
Dr Lorna Fern	Research Development Coordinator	London
Dr Tom Maishman	Statistician	Southampton
Mr Benjamin Thomas	Urologist	Cambridge

* denotes trainee member

Further Membership information

Anna Castleton aims to examine the clinical outcomes after TYA allograft transplantation, and to work on the return of patients to their workplace after acute lymphoblastic leukaemia.

Ben Carpenter aims to work alongside Dr Castleton on transplant outcomes in TYAs, and also continue to study the treatment pathways and outcomes of TYA with non-Hodgkins lymphoma working with our previous member Professor Carr.

Julia Chisholm aims to work on sarcoma outcomes, clinical trials, and biology within the Biological Studies Subgroup.

Louise Soanes aims to work on under-represented minority groups among TYA including the outcomes for patients from ethnic minorities, with Richard Feltbower and others.

Carla Reid aims to work on rehabilitation outcomes after TYA cancer.

Nicola Petit aims to work on public engagement, and carer engagement.

Bethan Ingram aims to work on fertility after TYA cancer from a nursing perspective.

Richard Feltbower aims to work on the epidemiological analysis of TYA cancer outcomes from cancer registry and other forms of big data, link this to GCT outcomes, the educational outcomes after treatment in our patient group, and brain tumour outcomes.

Sarah Pratap from Oxford has been appointed as the new chair of the Biological Studies Subgroup. Sarah has experience as a research active clinician and a member of the Sarcoma CSG.

We wish to welcome our new trainee members. Each of our trainee members have mentors who they have met for advice and support.

Nicola Pettitt, from Birmingham. Nicola's specific role is at this time in relation to patient and public engagement where she is developing a novel model for that, in collaboration with the germ cell charities and Lorna Fern.

Hadeel Hassan, from Leeds, is specifically focusing upon the messaging that comes out of our clinical studies group to our wider clinical and research community. We have designed and are preparing to implement awareness surveys to our clinical community to understand our impact as a clinical studies group, and now we can serve the needs of our clinical community better.

Membership of the Subgroups Membership of the Subgroups

Biological Studies Subgroup		
Name	**Specialism**	**Location**
Dr Dan Stark	Medical Oncologist	Leeds
Dr Chris Barton*	Paediatric Oncologist	Liverpool
Dr Angela Jesudason**	Paediatric Oncologist	Edinburgh
Dr Martin McCabe (Outgoing Chair)	Paediatric Oncologist	Manchester
Dr Maria Michelagnoli**	Paediatric Oncologist	London
Dr Matt Murray	Paediatric Oncologist	Cambridge
Dr Bob Phillips	Paediatric oncologist	Leeds
Dr Frederik van Delft	Paediatric Oncologist	London
Dr Shaun Wilson	Paediatric Oncologist	Oxford
Dr Rachael Windsor**	Paediatric Oncologist	London
Dr Gareth Veal	Pharmacologist	Newcastle
Professor Sue Burchill	Professor of paediatric and adolescent cancer research	Leeds
Dr Lorna Fern**	Research Development Coordinator	London
Dr Kenneth Rankin	Surgeon	Newcastle

Health Services Research Subgroup		
Name	**Specialism**	**Location**
Mr Max Williamson	Consumer	Bedford
Dr Lisa McCann	Lecturer	Strathclyde
Dr Dan Stark	Medical Oncologist	Leeds
Ms Sue Morgan	Nurse	Leeds
Dr Rachel Taylor	Nursing/Clinical Trials	London
Dr Rebecca Ling*	Paediatric Oncology Trainee	London
Dr Lorna Fern (Chair)	Research Development Coordinator	London
Dr Anne-Sophie Darlington	Senior Research Fellow	Southampton

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

Survivorship Subgroup		
Name	**Specialism**	**Location**
Dr David Cutter	Clinical Oncologist	Oxford
Mr Max Williamson	Consumer	London
Professor Mike Hawkins (Chair)	Epidemiologist	Birmingham
Dr Bethan Ingram	Nurse Practitioner	Cardiff
Professor Hamish Wallace	Paediatric Oncologist	Edinburgh
Mrs Carla Reid	Physiotherapist	London
Professor Diana Greenfield	Professor of Oncology Nursing	Sheffield
Dr Danish Mazhar	Medical Oncologist	Cambridge
Dr Raoul Reulen	Senior Lecturer	Birmingham

* denotes trainee member
**denotes non-core member

Appendix 2

TYA & GCT Group & Subgroup Strategies

A – TYA & GCT Group Strategy

The Teenage and Young Adult and Germ Cell Tumours (TYA & GCT) Clinical Studies Group (CSG) 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 CSG will work collaboratively within our groups, between our groups under several research themes:

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

Groups: Delivering a portfolio of research

<u>Aims of the TYA and Germ Cell CSG:</u>

1. Ensure that teenagers and young adults are considered for and have opportunities to enter disease-specific NCRI CSG research studies; 'Trials'
2. Develop clinical trials for GCT for all stages of disease; 'GCTs'
3. Research into the optimal provision of health care for TYA (16-39 years) and to provide the evidence base for the present and future guidance for young people with cancer; 'Health Care Provision'
4. Further describe tumour and host biology and facilitate opportunities for personalised medicine in TYA; 'Biology'
5. Address survivorship and quality of life issues; 'Survivorship'

6. Enhance joint working within the TYAG NCRI group, between our subgroups, and with other NCRI groups

7. To influence and assess our impact as a CSG.

8. To ensure our research agenda is set to include young people who have experienced a germ cell tumour

Objectives of the cross-cutting TYA & GCT CSG:

1. The formation and successful running of a new subgroup in germ cell tumours

2. Biology

    - To develop a national research study examining TYA age, physiology and fertility outcomes after cancer and its treatment

3. Trials

    - To implement research into artificial intelligence and machine learning technology that enhances TYA and germ cell cancer research

4. Joint working

    - To make structural changes that promote all UK germ cell and TYA research studies being discussed at the TYAG CSG, and through that to maximise the inclusion of studies on the NCRI portfolio

    - To further enhance the co-development of our research with other NCRI research groups, by the identification of TYA leads within site-specific CSGs

    - To develop a pan-CSG system of integrating the patient view into research designs

5. To improve the external messaging of the CSG

Milestones and outputs of the cross-cutting TYAG CSG

Project	Lead individual	Others involved	New or continuing project?	Milestone	Milestone Date	Output	Output date
Form a germ cell subgroup	Jonathon Shamash	none	New	Application submitted	Sep-18	Subgroup met	Mar-19
Evolve the main group meeting	Dan Stark	none	New	New agenda agreed and used	Dec-18	New Agenda Evaluated	Dec-19
Identify TYA leads for key SS CSGs	Dan Stark	NIHR	continuing	First CSG TYA lead named	Oct-18	1st study submitted with JLA issue as substudy	Jun-21
Answer a JLA TYA question in a site specific clinical trial	TBC	Other SS CSGs	New	Engagement with a SS CSG TYA lead	Oct-18	Open a study addressing a JLA TYA question	May-21
Influence the NHS processes that deliver trial recruitment	Lorna Fern	NHSE CRG	continuing	none	none	comment on NHSE Service Spec	Dec-18
Digital interventions artificial intelligence and machine learning	Dan Stark	HSR subgroup, biology subgroup	New	Agree digital platform with a commercial or academic partner	Mar-19	workshop on digital data and artificial intelligence	Nov-19
Consumer involvement improved	Lorna Fern	germ cell Charities, GC SG, HSR SG	Continuing	Meeting with Germ cell nursing	Sep-18	Test new model on germ cell MiRNA study	Mar-19
Available recruitment data for TYA into trials	Dan Stark	NIHR	continuing	Edge database amended	Nov-18	Trial data presented to main CSg	Dec-19
Study of fertility after AYA cancer	TBC	Germ cell SG, biology SG, HSR SG	New	Study design group formed	Dec-19	Study design with pilot data presented to CSG	May-21
Messaging enhanced from CSG	Dan Stark	none	New	none	none	Messaging sent second time	May-19
Data about impact of the TYAG CSG	Martin McCabe	NCRAS	New	Identify existing NCRAS and patient survey data which addresses research	Dec-20	Further surveys of impact of CSG designed	Jun-21

Overall purpose of each Subgroup

- Contribute to the overall aims of the CSG
- Develop and deliver studies relevant to TYA cancers in their own field of expertise
- Deliver its part in the projects of the main CSG
- To work collaboratively, developing specific elements within their field of expertise, that can be taken forward as national collaborative projects by the main CSG and others

B – Biological Studies Subgroup Strategy

Specific aims:

- 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

Specific Objectives:

- 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

Milestones and outputs of the Biology SG

Project	Lead individual	Others involved	New or continuing project?	Milestone	Milestone Date	Output	Output date
Personalised medicine studies	Martin McCabe	EORTC	continuing	Meet including NGSeq expert	Aug-18	Proposal for personalised medicine trial	May-21
CCLG tissue bank	TBC	CCLG	continuing	qualitative data from cclg centres	May-19	New study design	May-20
Radiobiology and age	Dan Stark	CTRAD	New	New leadership group after workshop with CTRad	May-19	Protocol for TYA RT study	May-20
Pharmacology and age	Gareth Veal	Dan Stark, ECMC	New	Meeting with ECMC	Dec-18	Design for systematic review of PK and age	Dec-19
Dose intensity funded	Dan Stark	none	continuing	funding submitted to NIHR	Jan-19	none	none
identify new chair for subgroup	Dan Stark	none	New	none	none	new chair in post	May 2019

C – Germ Cell Tumour Subgroup Strategy

Aims:

- 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

Objectives:

- 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 CSG 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

Projects of the Germ cell subgroup

Project	Lead individual	Others involved	type	Milestone	Milestone Date	Output	Output Date
Studies to reduce toxicity and maintain efficacy	Jonathon Shamash	none	continuing	Studies discussed in the new group	Jun-19	submission for funding	Mar-20
Stratified treatment in resistant disease	Andrew Protheroe	MAGIC	New	none	none	funding application	Dec-19
CXC-12 study	Robert Huddart	none	continuing	none	none	funding application	Dec-18
the implementation of micro-RNA in germ cell tumour management	Matt Murray	MAGIC, G3	continuing	none	none	Proposal for NHS implementation	May-20
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

D – Health Services Research Subgroup Strategy

Aims:

- 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

Objectives:

- To lead in assessing emerging structural changes in trial approval processes and infrastructure, using high quality research designs
- Address priorities agreed in the James Lind Alliance in collaborative national research studies
- Examine the interaction between TYA patients, as they mature psychologically and behaviourally, and health care systems notably in the field of pathways to diagnosis
- Seek funding for further development of the BRIGHTLIGHT study
- Examine how digital health interventions can be used to improve patient experience and clinical trial recruitment
- To undertake developmental studies, building towards national and international research into end of life care in TYA and germ cell tumours

Milestones and outputs of the HSR SG

Project	Lead individual	Others involved	type	Milestone	Milestone Date	Output	Output date
Use the JLA to influence funding	Lorna Fern	The JLA leads	New	Meet with funders	Nov-18	Meeting with charity funders	Nov-19
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
The impact of TYA age on pathways to diagnosis	Lorna Fern	none	Continuing	Include systems research and logic modelling in the HSR subgroup	May-19	Present the designed programme to the main CSG	May-20
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 HSR subgroup	Jul-19	Present the designed evaluation to the main CSG	Jul-20

E –Survivorship Subgroup Strategy

Aims:

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

Objectives:

- 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 and health services research subgroups
- To contribute to studies of fertility led by the main CSG

Milestones and outputs of the Survivorship SG

Project	Lead individual	Others involved	type	Milestone	Milestone Date	Output	Output date
Cerebrovascular Case-control study	Mike Hawkins	CCLG RT group	New	none	none	funded	May-20
New TYACSS linkages	Mike Hawkins	none	New	Present possibilities for Fertility data linkage	Mar-19	none	none
Plan germ cell LE analyses	Mike Hawkins	Germ cell SG	New	Agree key areas with GCT subgroup	Jan-19	Analysis of one key areas	Sep-19
Develop new models of follow up evaluation or trial	Danish Mazhar	Germ cell SG	continuing	App partner agreed	Mar-19	study design to CSG	May-20

Themes: Bringing together subgroups, working across them

Theme 1 - trials

Evaluate the impact of changes in TYA research national structures	Influence the NHS processes that deliver trial recruitment	Consumer involvement improved in trial design	Identify TYA leads for key SS CSGs
HSR Subgroup leading	Main CSG leading	Main CSG leading	Main CSG leading
Lead researcher TBC	Lead researcher Lorna Fern	Lead researcher Lorna Fern	Lead researcher Dan Stark

Theme 2 – Biology

facilitate personalised medicine for TYA with cancer Biology Subgroup leading Lead researcher Martin McCabe	explore the impact of dose intensity upon TYA outcomes Biology SG leading Lead researcher Dan Stark	expand access to biological samples of TYA cancers Biology SG leading Lead researcher Martin McCabe	To examine age variations in radiobiology Biology SG leading Lead researcher TBC
To examine age variations in pharmacology Biology SG leading Lead researcher Gareth Veal			

Theme 3 – Healthcare Provision

Age and GCT outcomes	The JLA to influence funding	Pathways to diagnosis	Evaluation of existing specialist TYA services
GCT Subgroup leading	HSR SG leading	HSR SG leading	HSR CSG leading
Lead researcher Richard Feltbower	Lead researcher Lorna Fern	Lead researcher Lorna Fern	Lead researcher Rachel Taylor

TYA Trial recruitment data from all NHS trusts to NIHR

Main CSG leading

Lead researcher
Dan Stark

Theme 4 – Survivorship

National cohort studies of TYA cancer survivors adverse outcomes

Surv SG leading

Lead researcher
Mike Hawkins

Nested case-control studies - risk factors for adverse outcomes

Surv SG leading

Lead researcher
Mike Hawkins

Extend data linkage of the TYACSS cohort

Surv SG leading

Lead researcher
Mike Hawkins

Fertility Studies

Main CSG leading

Lead researcher
TBC

Late Effects studies GCTs

Surv. SG leading

Lead researcher
TBC

Follow-up care GCTs

Surv. SG leading

Lead researcher
Danish Mazhar

Theme 5 - GCTs

	New therapeutic studies Germ cell SG leading Lead researcher One per protocol	New biomarker studies Germ cell SG leading Lead researcher One per protocol	Timely recruitment to existing national trials Germ cell SG leading Lead researcher Jonathon Shamash

Late Effects studies Surv. SG leading Lead researcher TBC	Fertility Studies Main CSG leading Lead researcher TBC	Age and GCT subgroups studies Main CSG leading Lead researcher Richard Feltbower	PPE evolution Main CSG leading Lead researcher Sue Brand	Follow-up care Surv. SG leading Lead researcher Danish Mazhar

Theme 6 – Joint working

Make the CSG accessible to all conducting TYA research	Adjust the agenda of the main CSG	Evolve the membership and their contribution	Develop joint trials with SS CSGs
Main CSG leading	Main CSG leading	Main CSG leading	Main CSG leading
Lead researcher Dan Stark	Lead researcher Dan Stark	Lead researcher Dan Stark	Lead researcher Dan Stark

Theme 7 – Impact

Create digests of CSG meetings	Multimedia presence for the CSG	Evaluate our impact as a CSG
Main CSG leading	Main CSG leading	Main CSG leading
Lead researcher Dan Stark	Lead researcher Dan Stark	Lead researcher Martin McCabe

Appendix 3

Portfolio maps

TYA

http://csg.ncri.org.uk/portfolio/portfolio-maps/- there are 27 maps for this cross cutting area.

Testis

See next page.

NCRI Portfolio Maps

Testicular Cancer

Map A – Germ cell tumours

ê below to reset map

		Advanced disease - 1st line	Biology and genetics	Early stage	Follow-up and quality of life	Salvage therapies
Non-seminomatous germ cell t..	All	TIGER UK P3BEP Trial	100,000 Genomes Project Bioresource (Main phase)		Late CT Study Vascular Effects of Chemotherapy for Testicular Cancer Latent Vascular Effects of Chemotherapy for Testicular Cancer Balance after chemotherapy Long-term balance after chemotherapy (LTBAC)	EA/001
Seminomatous germ cell tumours	All	TIGER UK P3BEP Trial	100,000 Genomes Project Bioresource (Main phase)		Vascular Effects of Chemotherapy for Testicular Cancer Latent Vascular Effects of Chemotherapy for Testicular Cancer Balance after chemotherapy Long-term balance after chemotherapy (LTBAC)	

Filters Used:
Active Status: All, **CSG Involvement**: All, **Funding Type**: All, **Phase**: All, **LCRN**: None

In Setup / single re.. Open / single rese..
In Setup / multi res.. Open / multi resea..

Appendix 4

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	CSG involvement in the trial
1. TYACSS: Bright, C.J., Reulen, R.C., Winter, D.L, Stark D.P., McCabe M.G., Jesudason A.B., Frobisher, C., Hawkins, M.M. Risk of subsequent primary neoplasms in survivors of adolescent and young adult cancer: The Teenage and Young Adult Cancer Survivor Study – a population-based cohort study. 2019 Feb 20. pii: S1470-2045(18)30903-3. doi: 10.1016/S1470-2045(18)30903-3. [Epub ahead of print]	Fundamental reconsideration of the aetiology and nature of second malignant neoplasms after TYA cancer, towards lifestyle causes and away from iatrogenic causes that are prominent in younger children	Idea, Design, Funding, Implementation (Hawkins and others)
2. Stark, D., Fern, L. A., Gibson, F., Hawkins, M., Hough, R., McCabe, M. G., & Taylor, R. (2018). Transitioning adolescent and young adult cancer care research out of its adolescence. European Journal of Cancer Care, 27(6). doi:10.1111/ecc.12962	The need for wider collaboration to develop the field of TYA cancer research	Idea, Design, Funding, Implementation (Whelan and others)

3. BRIGHTLIGHT: Taylor RM, Whelan JS, Gibson F, Morgan S, Fern LA. (2018) Involving young people in BRIGHTLIGHT from study inception to secondary data analysis: insights from 10 years of user involvement. Research Involvement and Engagement 4:50 doi: 10.1186/s40900-018-0135-x. Res Involv Engagem. 2018 Dec 27;4:50.		Idea, Design, Funding, Implementation (Whelan and others)
4. TE3. Development of a best-practice clinical guideline for the use of bleomycin in the treatment of germ cell tumours in the UK. Watson RA De La Peña H, Tsakok MT, Joseph J, Stoneham S, Shamash J, Joffe J, Mazhar D, Traill Z, Ho LP, Brand S, Protheroe AS. Br J Cancer. 2018 Oct;119(9):1044-1051. doi: 10.1038/s41416-018-0300-x. Epub 2018 Oct 25.	Improvements in the detection and management of this key and sometimes acutely fatal toxicity of germ cell tumour therapy	Idea, Design, Funding, Implementation (Shamash and others)
5. BRIGHTLIGHT: Fern LA, Taylor RM. (2018) Enhancing accrual to clinical trials of adolescents and young adults with cancer (invited review). Pediatric Blood and Cancer. Doi:		Idea, Design, Funding, Implementation (Whelan and others)

10.1002/pbc.27233. Pediatr Blood Cancer. 2018 Sep;65(9):e27233. Epub 2018 May 11		

Appendix 5

Recruitment to the NIHR portfolio in the reporting year

In the TYA & GCT CSG portfolio, 5 trials closed to recruitment and 8 opened.

Summary of patient recruitment by Interventional/Non-interventional

TYA

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2012/2013	269	-		257	-	-
2013/2014	661	0	619	0	-	-
2014/2015	497	0	476	0	-	-
2015/2016	190	5	138	5	-	-

Testis

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2012/2013	1342	277	1335	259	59.8	12.4
2013/2014	1639	290	1495	290	67.0	13.0
2014/2015	1349	140	1269	140	56.9	6.3
2015/2016	752	20	686	20	30.73	0.90

TYA & GCT

Year	All participants		Cancer patients only		% of cancer patients relative to incidence	
	Non-interventional	Interventional	Non-interventional	Interventional	Non-interventional	Interventional
2016/2017	872	6	639	6	-	-
2017/2018	321	193	231	193	-	-
2018/2019	502	384	415	365	-	-