NCRI
National
Cancer
Research
Institute

NCRI Teenage and Young Adults and Germ Cell Group

Annual Report 2019-20

Partners in cancer research

The NCRI Group Annual Reports 2019/2020 span the time period April 2019 – March 2020. The reports were submitted during a challenging time for all in the healthcare sector due to the COVID-19 pandemic. This has had an unprecedented impact on the activity of both the Research Group itself and wider research activities, ranging from the time available for research work versus clinical commitments to the funding of new trials and the recruitment of existing trials. Due to this the NCRI significantly extended the deadline for submission of annual reports and allowed the Groups to submit reduced reports, if time permitted, with the following sections at a minimum:

- Achievements (section 1 of the report)
- Funding Submissions over the last 12 months (section 5)
- Priorities and Challenges (section 7)

In addition to this, Consumer representatives of each Group were asked to only complete their sections if they feel able to. Most of our Consumers have submitted reports, however where reports have *not* been submitted this was due to extended periods of ill health, or additional work/home life constraints, as a result of COVID-19.

NCRI Teenage and Young Adult and Germ Cell Cancer Group
Annual Report 2019-20

1. Top 3 achievements in the reporting year

Achievement 1

Completion and dissemination of the BRIGHTLIGHT study has occurred during the last reporting year. This study was conceived in 2008, developed and implemented within the Teenage and Young Adult Health Services Research Subgroup and is a manifestation of over a decade of work by the Group. The cohort profile was published in the BMJ open and we are currently responding to minor amendments of the final manuscript of the primary outcome measure.

The current study results will have a clear specific impact upon practice & policy. To consolidate that impact we have proposed to the NIHR Policy funding stream a rapid evaluation of current Teenage and Young Adult Services and outcomes, updating BRIGHTLIGHT. This is submitted for stage 2. The policy proposal also includes detailed study of the links between specialist TYA centres and surrounding hospitals. The study will be jointly led by Subgroup Chair Dr Lorna Fern and Dr Rachel Taylor.

Achievement 2

Maintaining momentum of the success of the survivorship Subgroup last year and the publication in the Lancet Oncology in 2019 of the second malignant neoplasms analysis from the UK TYA cancer survivorship cohort study, the survivorship subgroup have secured additional grant funding to deliver impact in the NHS from these results. This reporting period we began the risk factor assessment study in brain tumours in TYA and received further new funding to "Establish a comprehensive surveillance system for adverse health outcomes in British survivors of childhood, teenage and young adult cancer." The three-year study to February 2023 is led by Subgroup Chair Professor Mike Hawkins.

Achievement 3

SPECTA AYA opened during our reporting period 2018-2019. During the reporting year this international study recruited 50 high grade sarcomas, mainly osteosarcoma and Ewings sarcoma and 50 high grade gliomas. The initial aim has been exceeded - feasibility assessment of sample collection and pilot data. Moreover, there have been individual patient impacts including; access to personalised trials based on sequencing results (i.e. e-SMART); the detection of a previously unknown mismatch repair defect; a change in diagnosis; compassionate use drugs accessed. Further funding has been sought, and this is forming part of a proposal to the Experimental Cancer Medicine research community.

2. Structure of the Group

No new structural changes this period.

Membership changes: Consumer Lara Veitch died from her cancer in May 2020. Lara was an active member of the RG, the HSR Subgroup, BRIGHTLIGHT and the TYA JLA. We dedicate this report to her delightful memory.

Departing members: We are hugely grateful to Dr Martin McCabe former Chair of the Biological Studies Subgroup and Dr David Cutter.

New members: Dr Graham Wheeler, statistician from the Cancer Research UK & UCL Cancer Trials Centre; Dr Julia Chisholm, Paediatric Medical Oncologist and Chair of the NCRI Children's Group.

Trainees; Ms Nicky Pettit continues as an active member of the HSR Subgroup. Her research interests are on carers and she is utilising her time on the Group to contribute to her academic MSc. Her thesis includes secondary data analysis of BRIGHTLIGHT carer data. She has led on a publication on clinical trial entry which is under review. Dr Hadeel Hassan is measuring the impact of the Group in our community and has disseminated a baseline survey. Her PhD thesis on preventable deaths in TYA with cancer is submitted.

The chair and other members have built further specific international links this period, including with ESMO, SIOPE and EONS formally and with ESH informally, around TYA cancer research. Consensus is developing between these powerful organisations as to priorities and joint working. Several of our trials are developed with international organisations such as US Children's Oncology group, EORTC, ANZUP and similar groups in India, China, Brazil and Japan.

Many of the Research Group members have been redeployed during COVID-19, reducing their research. This was to be the year of the AYA Global Congress in London, led by 2 RG members, until coronavirus intervened. Now this will be July 2021, we hope.

3. Teenage and Young Adult and Germ Cell Cancer Group & Subgroup Strategies

Teenage and Young Adult Germ Cell Cancer Group

The Group and the four subgroups have a set of an inter-related strategic aims, objectives and specific projects, and a balance between age-related and germ cell specific projects.

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

This study, led by Professor Hamish Wallace and Professor Anderson in the world-leading Edinburgh centre, is funded by a commercial partner and staff are recruited. It is delayed opening under COVID-19. It will seek to comprehensively evaluate reproductive function in TYA in selected centres, generating new evidence for the gonadal toxicity of existing and novel agents, validating new risk algorithms for fertility reduction, and examining novel biomarkers. If successful in selected centres we aspire that it will extend to all-centre all-TYA reach. The group have reviewed French and Irish national proposals this reporting period, building international links.

Understanding TYA Radiotherapy outcomes

With the support of the NCRI we were delighted to host a joint workshop with CTRad, the TYA and CCLG Radiotherapy Group in Leeds in June 2019. The meeting brought together key professionals (including the NIHR sub-specialty lead for radiotherapy) beyond our normal sphere and was an excellent opportunity to further strengthen links within the wider oncology and radiotherapy environment. More importantly, the workshop generated three outline projects, with the potential of involvement of our subgroups in two. This includes a shared understanding of planned proton beam therapy research/evaluations proposed in Manchester and London.

Developing further research into the clinical pharmacology of TYA with cancer.

This is now beginning to extend beyond the work of Veal on pharmacology in Ewing sarcoma and the work of Stark/Feltbower/Hughes on drug dosing and outcome in TYA. The group is developing a proposal to the ECMCs to study and improve the engagement of TYA with cancer in Experimental Cancer Medicine Centre (ECMC) studies. This is timely, building upon the developments for clinical trial recruitment that are active in the NHS service specification and the developments in measuring trial entry in the National Institute of Health Research (NIHR), plus the evolution in TYA-specific research nursing being led by the NIHR Comprehensive Local Research Networks (CLRNs.) The proposal is seeking the wide and strategic engagement it will need from the scientific, trialist, ECMC, Patient and Public Involvement and Engagement (PPIE) and clinical communities and hopes to come to fruition in 2021-22. The specific proposal is to include TYA issues in the renewal applications for ECMCs in 2021-2. At this point joint proposals are being co-written by the RG, ECMC leads, ACCELERATE leads, NHS England leads and other RG chairs, for discussion with funders.

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

The group now has formal links to named members of the site-specific Groups.

- Brain – Dr Martin McCabe
- Upper GI – Professor John Bridgwater
- Skin – Dr Miranda Payne
- Gynae – Dr Michelle Lockley
- Living With and Beyond Cancer – Professor Sam Ahmedzai
- Head & Neck – Mr Sabapathy Balasubramanian
- Breast - Dr Jean Abraham
- Children's – Dr Julia Chisholm and Dr Sara Stoneham
- Sarcoma – Dr Sarah Pratap
- Colorectal – Dr Andrew Beggs

We next plan to utilise this to ensure we are aware early of trials in development that will seek to recruit TYA, so that we can influence their design according to the known factors which enhance TYA enrolment, and nest sub-studies within some that address TYA-specific questions, such as around pharmacology or age-appropriate informed consent.

Trial participation in TYA as an applied health research project.

The Group is at the heart of the collaboration with NHS England, the NIHR and TYA cancer charities to improve clinical trial recruitment in TYA with cancer. Our role is the provision of studies. We have met each of the objectives we lead upon, from the 2019 summit. Our broad range of research grant applications specific to TYA, many successful, provides key groundwork. The improvements in infrastructure to approach TYA (such as research nursing), the improved scientific understanding of designing studies that are acceptable to TYA and planned improvements in the opening of studies for TYA in every NHS operational delivery network can develop upon this.

Biological Studies Subgroup (Chair, Dr Sarah Pratap)

The Biological Studies Subgroup appointed a new Chair Dr Sarah Pratap taking over from Dr McCabe. Additional members also joined the Group Dr Sam Behjati, paediatric oncologist and Sanger Centre faculty member, Dr Emma Woodward, clinical geneticist. The Group continues to make good progress against its strategic aims see below where we report on all our objectives (see appendix). Our highlights for this year include SPECTA completing recruitment, funding has

been successful for the dose intensity work and we held joint meeting with CTRAD, Children's Cancer and Leukaemia Group (CCLG) Radiotherapy Group and the TYA community.

From a successful pilot, plan personalised medicine intervention studies in TYA

SPECTA opened during our reporting period 2018-2019, recruiting TYA patients aged 12-29 with high grade gliomas and intermediate and high grade sarcomas. Over the past year the study has recruited 50 high grade sarcomas, mainly osteosarcoma and Ewings sarcoma and 50 high grade gliomas. The initial aim was to assess feasibility of sample collection and assess pilot data. However, there have been some individual patient benefits as patients have had access to personalized trials based on their sequencing results (i.e. e-SMART) and detection of unknown mismatch repair defect, also a change in diagnosis was discovered and compassionate use drugs were accessed at relapse. Recurring highly expressed genes in Ewings have also been identified which may be useful in approaching industry as a potential target. Further funding has been applied for to develop SPECTA. The ultimate aim is to develop a TYA Basket trial.

Dose intensity – A registry and pooled trial data analysis is funded

An NIHR Doctoral Training fellowship was obtained in this reporting period by Stark and Feltbower to train Dr Nicola Hughes to deliver this work within her PhD. Nicola has access to an international clinical trials dataset for TYA cancers, the National SACT dataset for TYA cancer and the regional specialist TYA cancer register dataset, enabling nested and increasingly detailed examination of the relation between systemic treatment delivered and dose intensity and clinical outcome. This work will complete in 2023. It includes international links to the European and US sarcoma and Germ cell trial communities.

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 and tissue banking is an ongoing priority for the biological studies subgroup. However, progress remains slow due to personnel changes/shortages. The Chair has had positive discussions with Mr Ashley Gamble at the Children's Cancer and Leukaemia Group, Mr Owen Burbridge the CCLG Tissue Bank Manager and Professor Deb Twededle, tissue bank director to progress this aim further. We intend to showcase Oxford as an example of how TYA tissue can be collected as well as paediatric. This will progress at a greater pace with the new mandate for TYA all to be offered the chance to bank tumour tissue under the 2020 NHS England Service Specification, and the new structure for Genomic analyses in some key TYA cancers, such as sarcoma.

Radiobiology, pharmacology, and age

With the support of the NCRI we were delighted to host a joint workshop with CTRad, the TYA and CCLG Radiotherapy Group in Leeds in June 2019. The meeting brought together professionals out of our normal sphere and was an excellent opportunity to further strengthen links within the wider oncology and radiotherapy environment. More importantly, the workshop generated three outline projects, with the potential of involvement of the BSG in two. One is a project on lung cancer as a second malignant neoplasm, being led by Professor Hawkins, and

the other is a project on circulating biomarkers during radiotherapy as predictors of end-organ toxicity, led by Dr Fiona Harris in Cambridge.

The existing PK/PD/PG study has now recruited 100 patients with Ewings Sarcoma who have had standard chemotherapy across ages. A further 15-20 patients are sought to complete recruitment due to difficulties with sample quality/processing in some samples. Initial analysis has shown differences for some drugs in the TYA population. Further funding has been sought for more in-depth analysis to be carried out.

Genomic medicine studies

New Group member Emma Woodford is developing an NIHR Fellowship proposal which will examine the prevalence of hereditary alterations in cancer predisposition genes in the teenage and young adult cancer population, implications of testing for young people, their families and how the NHS can best respond in terms of cancer management and future cancer risk. The proposal has a workstream dedicated to patient and public involvement and is led by Subgroup Chair Dr Fern. The proposal also has a workstream dedicated to psychological support need for young people and their families going through genetic testing.

Health Services Research (HSR) Subgroup (Chair, Dr Lorna Fern)

The subgroup has had another successful year with two face to face meetings, a number of teleconferences, five grant submissions and publications related to the portfolio. We have welcomed to new research group members onto the Subgroup, Dr Louise Soanes and our trainee Ms Nicky Pettit. We have links with the LWBC Group as Professor Sam Ahmedzai is a subgroup members. Mr Max Williamson has provided excellent consumer input and also provides a link to the survivorship subgroup. Sadly, Lara was unable to attend meetings in the last year due to sickness.

Ongoing evaluation of NHS services for TYA with cancer

Our NIHR Programme Grant BRIGHTLIGHT is completed and final results were presented during a three hour symposium at the annual TYAC Education day in November 2019 which was well attended by Subgroup members. We have published the profile of the Cohort in British Medical Journal (BMJ) open in April 2019 (10.1136/bmjopen-2018-027797) and the carers data in December 2019 (10.1097/NCC.0000000000000771). The paper detailing the primary outcome measure is under review, with survival and clinical processes nearing final draft for submission. 'There is a light' an evaluation of the dramatization of BRIGHTLIGHT is also under review.

Following funding from the NIHR in the last reporting period we recently appointed an analyst to carry out secondary data analysis to maximise the study outputs.

Our trainee Ms Pettit will carry out analysis of the carer data and will form the basis of her MSc.

A priority for the Subgroup and BRIGHTLIGHT team is to secure further funding based on the BRIGHTLIGHT results. Dr Fern and Dr Taylor are Co-Principle investigators of follow up study currently under review the NIHR (two stage process, £150k) to determine if current services would generate similar results to the current BRIGHTLIGHT study.

Existing BRIGHTLIGHT data is informing the design of many further studies. For example Professor Dan Stark (Chief Investigator) with Dr Taylor and others were awarded £1m from the Economic and Social Research Council to examine social reintegration of TYA following a cancer diagnosis. Part of the study will utilise existing BRIGHTLIGHT data and the creation of a new cohort. This study is in set up but is being impacted by COVID-19.

The impact of TYA age on pathways to diagnosis

The Group have successfully received funding from the Cancer Research UK Early Diagnosis and Advisory Committee to carry out secondary data analysis on the BRIGHTLIGHT Routes to Diagnosis and outcomes data. The 40K was awarded to LF as Principle Investigator and will continue the collaboration with the UCL's Epidemiology of Cancer Healthcare & Outcomes. An analyst has been identified and analysis will begin in the summer of 2020.

A second routes to diagnosis paper from BRIGHLTIGHT is currently under review with JAMA Open Network.

Use the JLA to influence funding

We published the final results of the JLA in BMJ open in June 2019 (10.1136/bmjopen-2018-028119). The paper has been downloaded over 3000 times, attracted a lot of social media attention and was picked up by press. The challenge now is to fit the priorities into the funding remits of existing funders, or work with funders in the development of funding strategies which reflect what young people, carers and professionals want. Researchers in the community have felt that the Top 10 has helped with funding successful applications and was probably also influential in the CRUK Grant. Although this is difficult to measure.

We hosted a meeting with relevant partners in September 2019, funded by NCRI and we were invited to the NCRI partners meeting to present the Top 10. We have close links with the LWBC group and will continue to work with all relevant stakeholders to ensure the Top 10 is not lost and funding avenues are secured.

We have recently 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 will be published shortly.

We have also analysed the free text answers to the survey and a paper is nearing completion for submission. The work is cited in many of the groups grant applications.

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

The Subgroup and the Research Group have good links with the NIHR CTYA trials initiative with many members represented at the second strategy day in April 2019, including Mr Williamson and also some of the BRIGHTLIGHT user involvement Group. The Subgroup have had plans for a while to evaluate the 'dedicated TYA' research nurses being implemented across the networks. Dr Fern and Dr Taylor submitted an NIHR Research For Patient Benefit proposal in the summer of 2019. This was rejected for being out of remit despite having consulted with the Research Design Service Prior to submission. The proposal will be reworked and submitted in July 2020.

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

The Survivorship Subgroup met face-to face in London on 6th June 2019 and plan a video conference meeting to take place June/July 2020. The group have made significant progress against their objectives this year.

New TYA Cancer Survivor Studies (TYACSS) linkages

A new grant began in 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, Principal Investigator Professor Hawkins, funded by The Brain Tumour Charity.

In March 2020 a new grant was awarded by Children with Cancer-UK to the value of £350k to "Establish a comprehensive surveillance system for adverse health outcomes in British survivors of childhood, teenage and young adult cancer." The grant is for 3 years and led by Professor Hawkins.

A new PhD student started with Mr Raoul Reulen and Professor Hawkins in October 2019 funded by a grant awarded by Public Health England (PHE) 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 that cancer survivors have been linked to GP prescriptions at a national level.

Plan germ cell LE analyses

Analysis is underway to investigate pregnancy and labour complications in female survivors of teenage and young adult cancer using the Teenage and Young Adult Cancer Survivor Study (TYACSS) cohort. In the TYACSS cohort there are 24,309 and 4885 5-year survivors of testicular and ovarian cancers, respectively. Another PhD student also started with Mr Reulen and Professor Hawkins in October 2019 to undertake this analysis.

Develop new models of follow up evaluation or trial

Work with Dr Danish Mazhar to develop his proposed study of remote (e.g. via online data portals) 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.
More generally Dr Stark has published in this period the safety and acceptability of using PRO-based clinical follow-up for survivors of TYA cancer.

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 Central Nervous System (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.

Just accepted for publication in the International Journal of Cancer is a comparable publication relating to survivors of childhood cancer showing 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

Additionally, an MRI (with MRA) study of those most at risk is planned to understand the mechanisms leading to stroke and potential opportunities for early intervention aimed at prevention.

Impact of Research

In terms of "Impact" the risk stratification tool, developed by Professor Hawkins as part of the National Cancer Survivorship Initiative, has been used by NHS England for the evaluation of every survivor of childhood cancer and separately every survivor of teenage and young adult cancer when seen in follow-up clinics throughout England. It is part of the new "Service Specification" for TYA – see electronic links:

URL 2 (Teenage and Young Adult Cancer Network) see page 12 in the document at:
https://www.engage.england.nhs.uk/consultation/teenager-and-young-adults-cancer-services/user_uploads/service-specification-tya-principal-treatment-centres-and-networks.pdf

Germ Cell Tumour Subgroup (Chair, Dr Jonathan Shamash)

Implementation of circulating microRNA assay into germ cell tumour management

The circulating microRNA technology developed by Dr Matthew Murray and others for germ cell tumours is undergoing extensive testing for health service implementation in a range of national and international settings, including in the AGCT1531 and UKP3BEP trials funded by CRUK previously and in set-up, the former having received regulatory approval in this reporting period. The clear translational potential for this work has been highlighted in a number of key reviews, including during the reporting period, e.g. 'Current clinical trials are addressing these potential uses, for example, AGCT1531 (NCT03067181) in which serum miRNAs are being measured in patients with localized or metastatic extracranial GCTs.' (Murray & Coleman, Nature Reviews Urology, 2019;Sep;16(9):505-506. This has also stimulated a novel methodological approach to PPIE and implementation science, below.

Patient and Public Engagement Improved

We have held a second patient involvement workshop within this reporting window, which was facilitated by Dr Fern and Dr Murray. The workshop ascertained consumer views of the acceptability of replacing routine CT Scans in follow up with microRNA blood detection. The initiative has led to strong links with the Germ Cell Support Group at St. Bart's. This opens the door for further consumer testing through this means. The results of the workshop are currently under review with British Journal of Cancer, on the basis of the novel methods applied, that combine PPIE methods with implementation science methods, and apply that in a pre-implementation setting to achieving behavioural change in service users, healthcare professionals, organisations and policy-makers. A further revised manuscript has been invited.

Age and GCT outcomes

This work is under discussion between Mr Richard Feltbower, Dr Shamash and others from UK routine NHS data. A paper analysing TYA outcomes in international Germ cell Trials within the MAGIC group is accepted with minor revisions in a large international journal, with authors including Stark, Dr Murray and Dr Stoneham from this Subgroup. Members of this Group contributed data to the 2019 revision of the international Germ Cell Consensus Group prognostic scoring, which emphasises the older cohort of germ cell adults now presenting, and the challenges managing them. This was presented at ASCO and is prepared for publications including subgroup members as co-authors.

Stratified treatment in resistant disease

The funding application for the use of biologically directed treatment for relapsed Germ Cell Tumours, by Dr Andrew Protheroe and others, was unsuccessful.

Studies to reduce toxicity and maintain efficacy

The AGCT 1531 funded RCT is examining reduced toxicity of equally efficacious treatments in the management of good prognosis advanced germ cell tumour. It is open to recruitment in the US, Japan and Brazil, but still awaiting first patient in the UK.

Extend the evaluation of CXC-12 as a prognostic and predictive biomarker in non-seminomatous GCTs

This project, arising from a Royal Marsden Hospital/Institute of Cancer Research (ICR) germ cell biology project, is confirmed as within the translational sub-study in the international Alliance for Cancer Gene Therapy (AGCT) 1531 trial, as a retrospective analysis upon collected tissue and data, dependent upon laboratory cost funding in due course.

New studies to build upon this work are in discussion within the group in relation to surgical outcomes and minimally invasive surgeries, as well as the management of late-relapsing GCT.

4. Task groups/Working parties

We have one working party, the Early Onset Carcinoma Working Party which addresses research in young people up to age 39, in keeping with our TYA remit and in line with international upper age definitions of young adulthood. The working party was previously Chaired by Dr Angela Edgar and has been taking over in the last reporting year by Dr Feltbower.

The remit of Early Onset Carcinoma Working Party is 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 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

Progress this year

During the past reporting year the task group have developed an analysis protocol to compare the epidemiology of carcinoma appearing in 0-39 years olds vs those aged 40 years and above and obtained approval and funding to extract the national dataset.

The aim of the study is to evaluate our current knowledge of clinico-pathological features of early onset breast, colorectal and ovarian carcinoma, in order to inform development of preventative, screening and management strategies, to improve outcomes. This was submitted to Public Health England (PHE) via the Office for Data Release in order to receive a data extract for analysis. This is expected by July subject to ratification by the Office for Data Release (ODR) panel. The data are planned to be analysed over the late Summer and Autumn, with a publication due to be submitted by early 2021.

5. Funding applications in last year

Table 2 Funding submissions in the reporting year

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Cancer Research UK					
May 2019					
DANTE-PET. Development of imaging biomarkers within DANTE (a randomised trial to evaluate optimal Duration of ANti -PD1 monoclonal antibody Treatment in patients with metastatic mElanoma)	Biomarker Project Award	Dr Ferdia Gallagher	Preliminary	We peer reviewed this study, which is in an increasingly important cancer for AYA	
XIP1: Hyperpolarised Xenon Imaging in Chemotherapy Induced Pneumonitis	Biomarker Project Award	Professor Fergus Gleeson	Not supported	We peer reviewed this study	
Aspirin Esomeprazole Chemoprevention Trial - EXension Long-term (AspECT EXceL); for the definitive risks vs. benefits.	CRC - Extension	Professor Janusz Jankowski	Not supported	We peer reviewed this study	
IMAGE-ID: Image-guided Multi-modal Annotation of Genetics and tumour micro-Environment In patients with Diffuse glioma	Experimental Medicine Award (full)	Dr Matthew Grech-Sollars	Not supported	We peer reviewed this study	
November 2019					
REMoDL-A: A Randomised Phase II Evaluation of Molecular Guided Therapy for Diffuse Large B-Cell Lymphoma with Acalabrutinib	Endorsement	Professor Andrew Davies	Supported	We peer-reviewed this study, in a key cancer type for TYA	

COLO-PREVENT; A platform for developing COLOrectal cancer PREVENTion therapies	Clinical Trial Award	Professor Karen Brown	Supported	This is a key area for TYA, building upon the work of Hawkins on the prevention of colorectal cancer as a second malignancy occurring in TYA after abdominal radiotherapy during childhood. We peer-reviewed the grant.	
Personalized Intensity-Modulated Therapy in Post-Pubertal Patients with Newly-Diagnosed Medulloblastoma (PersoMed-I)	Clinical Trial Award	Dr Martin McCabe	Not supported	Developed and submitted by a group member	
Re-irradiation with Arginine-Deprivation in patients with early-recurring Glioblastoma: A Phase 1 Trial. READER-1	Clinical Trial Award	Dr Matt Williams	Not Supported	We peer reviewed this study	
Using BH3 profiling to develop a biomarker assay for acute myeloid leukaemia sensitivity to venetoclax	Biomarker Project Award	Dr Karen Keeshan	Not supported	We peer reviewed this study	
INSPIRE - (Investigating National Solutions for Personalised Iodine-131 Radiation Exposure) Measuring absorbed dose to tumour and organs at risk following routine iodine ablation therapy	Biomarker Project Award	Professor Jonathan Wadsley	Not supported - Preliminary	We peer reviewed this study	
CHAPTer: A Randomised non-comparative, Open Label, Multi-Centre, Phase I/II Study Evaluating the Safety	Clinical Trial Award	Dr Graham Collins	Not Supported - Offered Endorsement	We peer reviewed this study	

and Clinical Activity of CHOP (Cyclophosphamide, Hydroxydaunorubicin, Vincristine and Prednisolone) in combination with ASTX-660 in the Front-line treatment for Peripheral T-cell Lymphoma					
DANTE-PET. Development of imaging biomarkers within DANTE (a randomised trial to evaluate optimal Duration of ANti-PD1 monoclonal antibody Treatment in patients with metastatic mElanoma)	Biomarker Project Award	Dr Ferdia Gallagher	Not supported	We peer reviewed this study	
ATOMIC-G: Pegargiminase (ADI-PEG 20), pemetrexed and cisplatin versus lomustine-based chemotherapy in recurrent isocitrate dehydrogenase wildtype glioblastoma: a phase II, randomised, multicentre trial	Clinical Trial Award	Dr Peter Szlosarek	Not supported	We peer reviewed this study	
EsPhALL 2017/COG AALL1631 International Phase 3 trial in Philadelphia chromosome-positive acute lymphoblastic leukaemia (Ph+ ALL) testing imatinib in combination with two different cytotoxic chemotherapy backbones	Clinical Trial Award	Dr Michelle Cummins	Supported	We peer reviewed this study	

Other committees					
Study	**Committee & application type**	**CI**	**Outcome**	**Level of Group input**	**Funding amount**
Establishing associations between diagnostic timeliness and clinical outcomes, quality of life and patient experience in young people with cancer: analysis of the BRIGHTLIGHT Cohort	Cancer Research UK Early Diagnosis Group	Dr Lorna Fern	Supported	Developed from HSR Subgroup strategy	£42K
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	Two stage Under 2nd review	Developed from HSR Subgroup strategy	£149,770
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	Two Stage Under 2nd review	Developed from HSR Subgroup Strategy	£1,974,206
Development of a Sarcoma Specific intervention to manage fear of recurrence	Sarcoma UK Living with and Beyond Cancer	Dr Rachel Taylor	Supported	Adopted	£80,389
What is the effectiveness of a change in NIHR service delivery to enhance recruitment of teenagers and young adults with cancer to research (RECRUIT_ME)?	NIHR Research for patient benefit	Dr Rachel Taylor Dr Lorna Fern	Not supported (out of remit)	Developed from RG strategy	£349,495.00
Cancer, Intimacy and Resilience: Using the arts & creative facilitation to support AYA (Adolescent and Young	British Academy of Arts Knowledge Frontiers	Dr Brian Lobel	Not supported	Developed from HSR Subgroup	£200,000

Adult) patients in understanding their post-cancer/post-diagnosis body, sexuality, intimacy and relationships.					
Establish a comprehensive surveillance system for adverse health outcomes in British survivors of childhood, teenage and young adult cancer.	Children with Cancer	Professor Mike Hawkins	Successful	Developed from Survivorship Subgroup	£350,000
Pilot Studies to investigate self-reported health behaviours of teenage and young adult cancer	Children with Cancer	Dr Raoul Reulen	Not supported	Developed from Survivorship Subgroup	£50,000
Clinical Pharmacology Studies to Optimise the Treatment of Teenagers and Young Adults with Ewing Sarcoma	Sarcoma UK	Dr Garath Veal	Under review	Developed from Biological studies Subgroup	£120,000
End of Life Care for Infants, Children and Young People: a mixed methods evaluation of current practice in England and Wales	NIHR HS&DR End of Life care.	Prof Lorna Fraser Co-I: Dr Richard Feltbower	Funded	Input from Dr Feltbower in relation to study design, methods and outputs. Part of HSR strategy	£1.3M.
Impact of radiotherapy on long-term survival and health care utilisation in children, teenagers and young adult with brain tumours	Children with Cancer	Dr Richard Feltbower	Unsuccessful	Developed from recommendations emerging from national radiotherapy workshop on CTYA, devised and led by Dr Feltbower.	£345,000
Is the survival of teenagers and young adults with cancer associated with the dose and intensity of chemotherapy that they receive? The use of existing healthcare datasets to answer the question.	NIHR Doctoral Training Fellowship	Prof Dan Stark, Dr Richard Feltbower	Successful	Developed within the RG from the biological SG	£450,000

6. Consumer involvement

Lara Veitch

Lara Veitch joined the TYA GC Group in January 2017 and sadly passed away in May 2020. She was delightful by character and an active member of the consumer forum, the Research Group, the Health Services Research subgroup, the BRIGHTLIGHT study and the Teenage and Young Adult James Lind Alliance Priority Setting Partnership. She also led on a project, supported by the Subgroup which she presented at the NCRI Conference 2017 and won the Social Impact prize by King's College London where she was studying. Prior to the death, she said she was grateful for the opportunity to have contributed to the research studies and she felt it was a very worthwhile thing for her to have done. Thank you to all of you in the Group who have supported her during the past three years.

Max Williamson

Max has been a consumer on the TYA/Germ Cell Tumour Research Group and Health Services Research Subgroup since September 2016, as well the Survivorship Subgroup since June 2018. In 2019, his role as Consumer on the Research Group was renewed for another three years. In this role, Max has contributed to the design of multiple different research studies and has been involved in grant applications for both subgroups and the committee as a whole, and (he hopes) has boosted the profile of the work of the Group at home and abroad. Max is a patient representative on two of the group's Trial Steering Committees, TIGER (since August 2017) and P3BEP (since May 2019), where he has worked to help the team improve patient-facing documentation and routes to accrual.

Within the Consumer Forum, in the last year Max has presented twice, at the meeting in May 2019 and at the November 2019 NCRI conference, on the cancer cell biology research he had helped with as part of his dissertation at UCL, with the second presentation being shared between him and his supervisor (who is also a cancer patient) on the role consumers can have in basic science research. Prior to the change in wind, Max was working with Emma Kinloch and Tim Humphrey in the Consumer Forum, to impact research productivity through creating an Oxford Dragon's Den Session for NCRI consumers, receive training, and deliver PPI on the doorstep of a biomedical research hub.

Within the UK, Max was a member of the steering group for the successful CCLG/MaGIC Germ Cell Tumour conference in September 2019 and was invited to be a part of the NIHR TYA Clinical Research Network (CRN) Steering Group Committee in November 2019. He is part of the Patient/Parent representative group for the CCLG imaging meta-analysis conducted by Dr Jess Morgan and Dr Bob Phillips and presented the results of this work with Jess at the UK TYAC Conference 2019, along with providing the 'patient voice' on a panel on research ethics in adolescent medicine at the same conference. Max has also begun work with Professor. Sheila Lane, conducting a patient-centred service evaluation of the Oxford Future Fertility Trust Services, which works with the Fertility team in Edinburgh to create an infrastructure of fertility preservation for young people with cancer across the UK.

Internationally, Max continues his work with the ACCELERATE FAIR Trials working group and is now a member of the Long-Term Follow Up Working Group too. In February 2020, Max presented at the ACCELERATE conference with representatives from the EMA, Janssen and the Royal Marsden/Experimental Cancer Medicine Centre (ECMC) on routes to regulatory approval in non-conventional clinical research like single arm trials, and the roles of the consumer in deciding what kinds of research are acceptable, ethical and practical; he also co-chaired a plenary session. Max was one of the few patient advocates who was invited to take part in the European Patient Forum's Summer Training Course for Young Patient Advocates, an online course focusing on representativeness, transparency and research ethics when involving young people and their families in research.

Lastly, Max has also been a co-author on three oncology papers since the last annual report;

- Matthews H.K., Ganguli S., Plak K., Taubenberger A.V., Win Z., Williamson M., Matthieu Piel., Guck J., Baum B., (2020) "*Oncogenic Signaling Alters Cell Shape and Mechanics to Facilitate Cell Division under Confinement*". Development Cell, 52, 563-573. DOI: 10.1016/j.devcel.2020.01.004

- Aldiss S., Fern LA., Phillips RS., Callaghan A., Dyker K., Gravestock H., Groszmann M., Hamrang L., Hough R., McGeachy D., Morgan S., Smith S., Upadhyaya S., Veitch H., Veitch L., Williamson M., Whelan JS., Gibson F., (2019) "*Research Priorities for Young People with Cancer: a UK Priority Setting Partnership with the James Lind Alliance*". BMJ Open, 9(8):e028119 Doi: 10.1136/bmjopen-2018-028119.

- Stoneham S., Murray M., Thomas B., Williamson M., Sweeney C., Frazier L., (2019) "*AYA Testis Cancer: The Unmet Challenge*", Paedatr. Blood Cancer, 66(2): e27796 Doi: 10.1002/pbc.27796

Max thanks the Research Group and the Consumer Forum again for all of their help and support, in particular to his Scientific Mentor Dr Lorna Fern, who has been crucial in helping him progress over the last four years.

Vincent Wolverson

No consumer report submitted – please refer to page 2.

7. Priorities and challenges for the forthcoming year

Priority 1

To build a working relationship for TYA with the ECMC research body. This can ensure TYA issues with trial enrolment are addressed from the beginning of the history of a cancer treatment. This can be highly collaborative, with ACCERELERATE 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 our 2018-19 feedback letter.

Priority 2

To open our TYA-specific trials, notably in fertility. This strengthens our industry relationship as requested in our 2018-19 feedback letter.

Priority 3

To innovate in PPIE, allowing a wider range of TYA to contribute without needing time away from work and education.

Challenge 1

Mitigating the impact of COVID19 on TYA and Germ Cell Research

The shortfall in charity funding; *Securing funding for studies:* The majority of our charitable funding bodies in the UK have been significantly impacted by the cut in fundraising activities during the COVID-19 pandemic, the national council for voluntary organisations have predicted up to 48% decrease in income. We anticipate this will negatively impact on the research funding opportunities for some time, with smaller funds available and increased competition.

Challenge 2

To embed ourselves further in the wider inter-organisational push for improved trial recruitment – now the NIHR, NHS England, ourselves, the age-specific and cancer specific charities, and we hope the Health Research Authority (HRA) and Medicines and Healthcare products Regulatory Agency (MHRA) can all work in unison on this. The lack of funding for the TYA research nurse posts within the NIHR Local Research Networks was a considerable setback for us – teams are working to moderate this impact locally, but it makes it very difficult to understand the potential to recruit to portfolio studies in TYA.

Challenge 3

Mitigating the impact of COVID19 on TYA and Germ Cell Research

The disrupted laboratory and clinical research landscape: *Recruitment to currently open studies*: The impact on recruitment to existing research studies as they reopen following suspension during the pandemic.

8. Collaborative partnership studies with industry

The national TYA reproductive function study, led by Professor Hamish Wallace and Professor Richard Anderson in Edinburgh and developed extensively in this RG, is funded by an Industry partner.

There is the potential for further industry partner research in implementation of micro-RNA in GCT, and in the use of commercial PRO platforms in TYA cancer outcomes.

9. Appendices

Appendix 1 A - Teenage and Young Adults and Germ Cell Cancer Group strategies
B - Biological Studies Subgroup Strategy
C - Germ Cell Tumour Subgroup
D - Health Services Research Subgroup Strategy
E – Quality of Life and Survivorship Subgroup Strategy

Dr Dan Stark (Teenage and Young Adults and Germ Cell Cancer Group Chair)

Appendix 1

A - Teenage and Young Adults and Germ Cell Cancer Group 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

Aims of the TYA and Germ Cell CSG:

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

B – Biological Studies Subgroup Strategy

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

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

C - Germ Cell Tumour Subgroup

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

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

E – Quality of Life and Survivorship Subgroup Strategy

Aims:

- To identify and characterise substantially elevated adverse health outcomes in TYA living after cancer

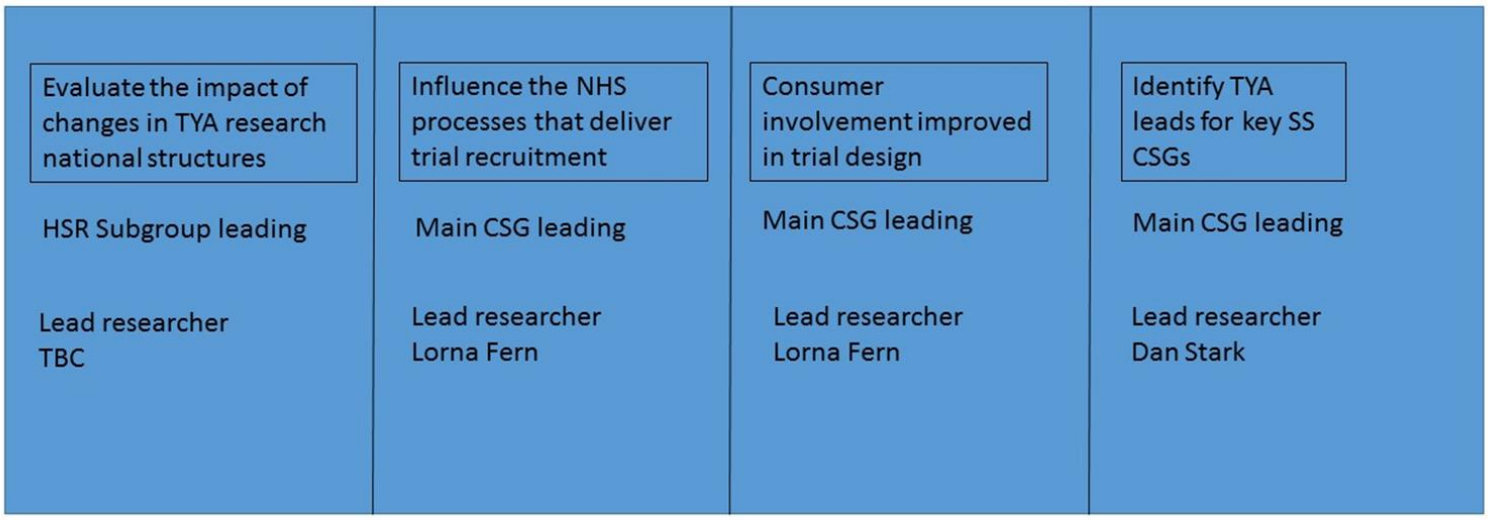
- To determine opportunities for prevention and other interventions aimed at risk reduction.
- To extend the available research data about TYA living after cancer
- To study models of NHS care for TYA living after cancer

Objectives:

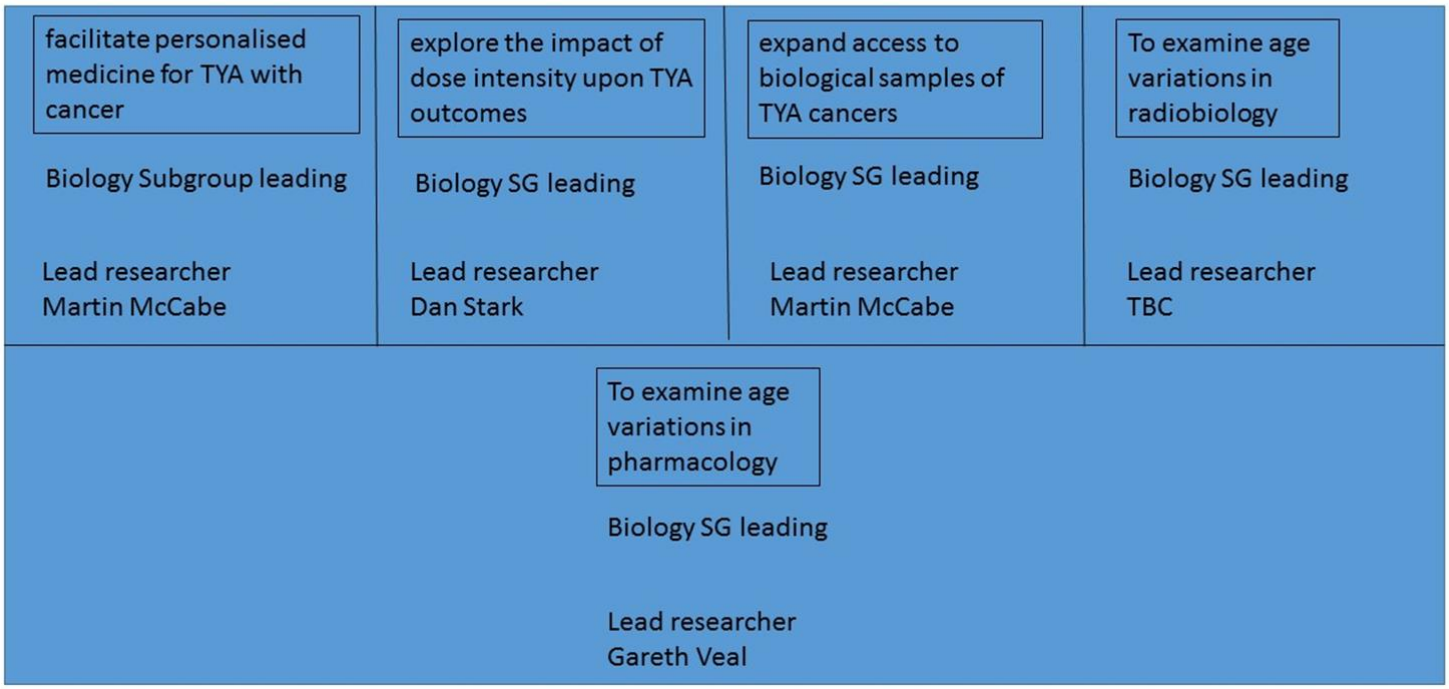
- To undertake a systematic programme of national population-based cohort studies of survivors of TYA cancer to identify adverse health outcomes with substantially increased risk
- To determine a comprehensive understanding of adverse health outcomes, using nested case-control studies to determine risk 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

Themes: Bringing together subgroups, working across the

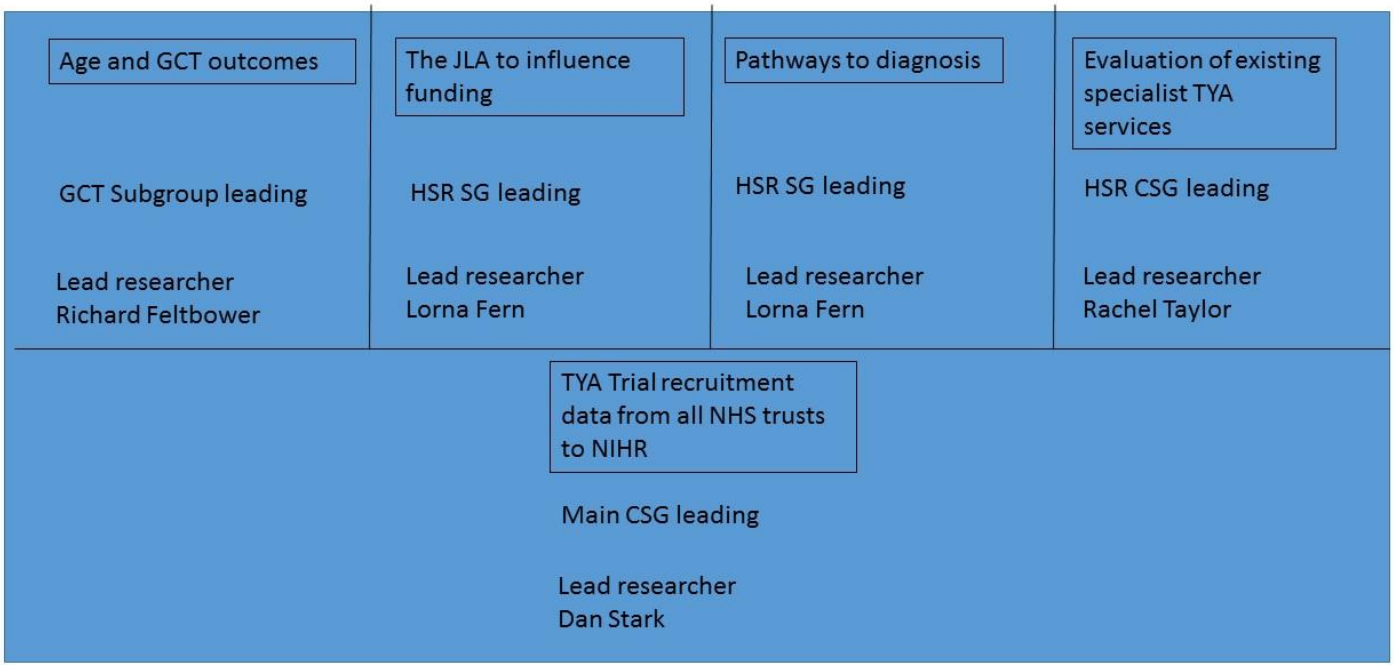
Theme 1 - trials



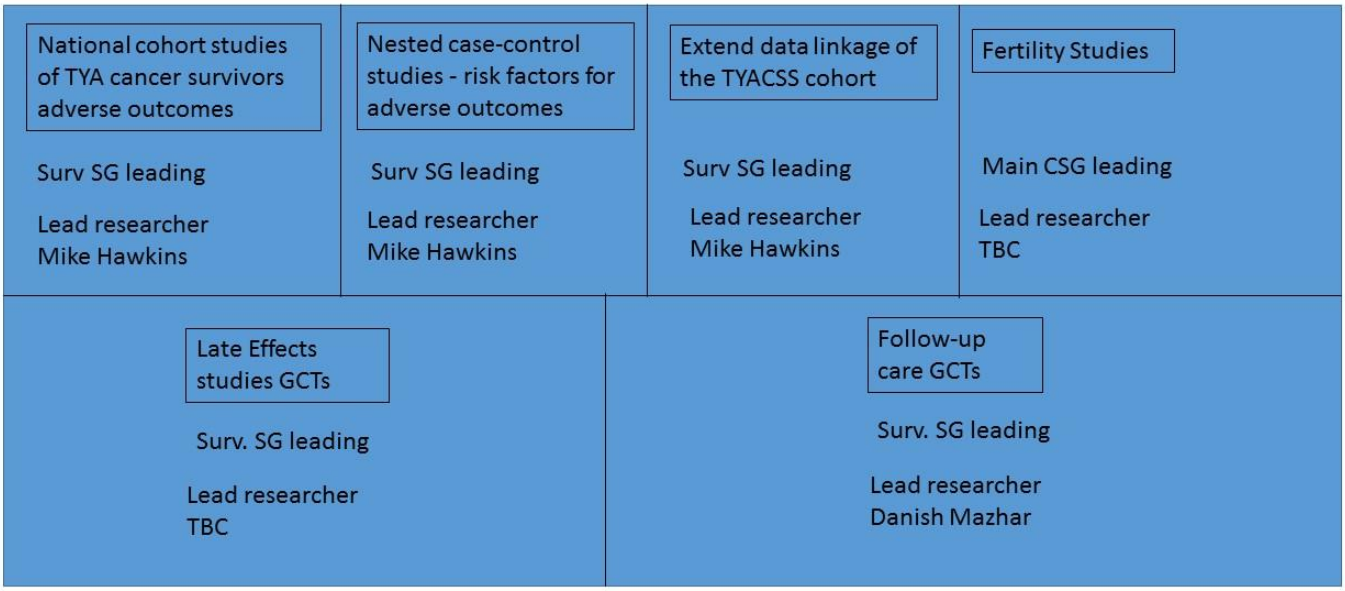
Theme 2 – Biology



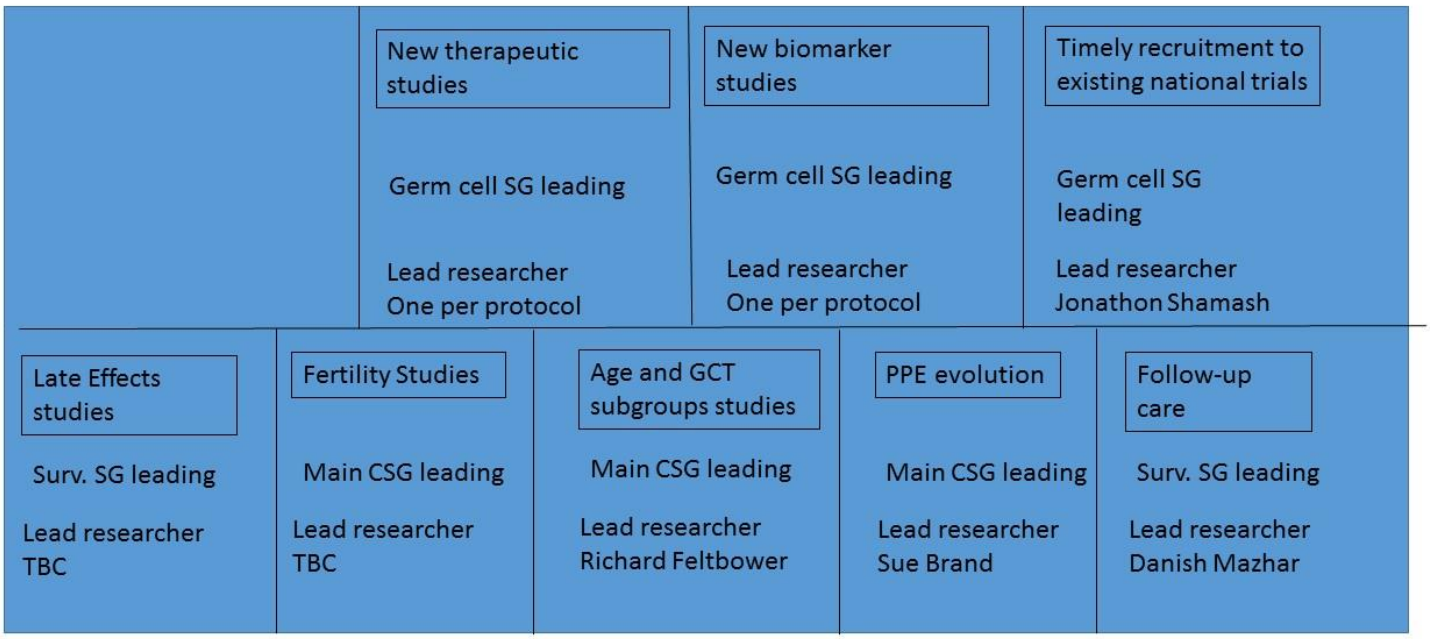
Theme 3 – Healthcare Provision



Theme 4 – Survivorship

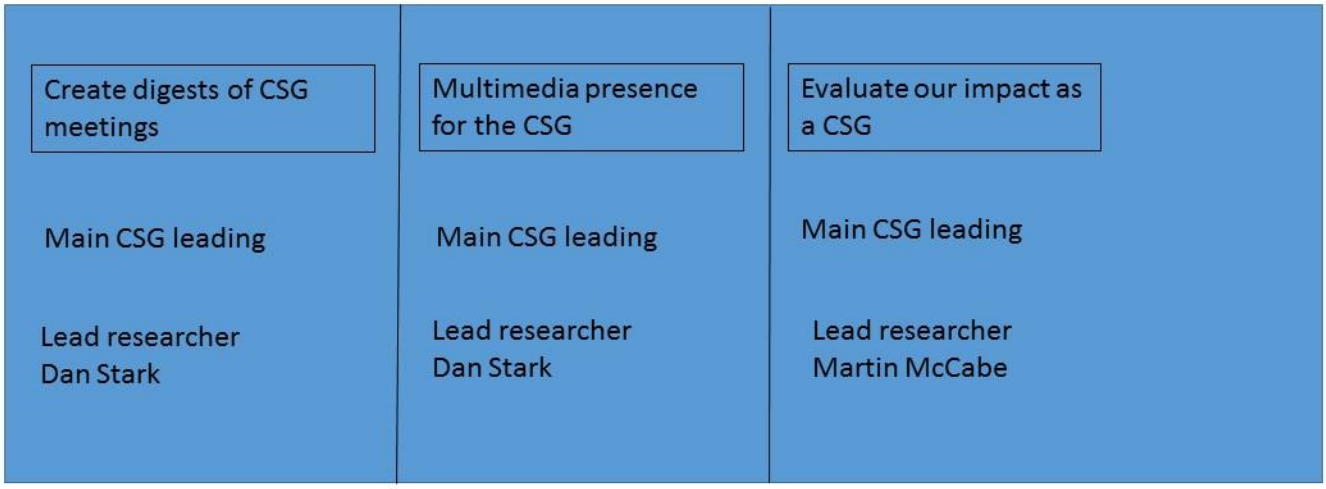


Theme 5 - GCTs



Theme 6 – Joint working

Theme 7 – Impact



Appendix 2

Top 5 publications in the reporting year

Trial name & publication reference	Impact of the trial	Group involvement in the trial
1. Aldiss S, Fern LA, Phillips RS, Callaghan A, Dyker K, Gravestock H, et al. Research priorities for young people with cancer: a UK priority setting partnership with the James Lind Alliance. BMJ Open. 2019;9(8):e028119.	Identified Top 10 Research Priorities for TYA. Considerable interest from UK funders.	Developed from Subgroup ~2013
2. Taylor RM, Fern LA, Barber J, Alvarez-Galvez J, Feltbower R, Morris S, et al., Stark D, Whelan J. Description of the BRIGHTLIGHT cohort: the evaluation of teenage and young adult cancer services in England. BMJ Open. 2019;9(4):e027797.	First publication of BRIGHTLIGHT Cohort and evaluation of specialist services for young people with cancer. NIHR policy application evaluating outcomes associated with new 'joint care' model proposed by NHS England.	Developed from feasibility study developed by subgroup in 2009 and successful NIHR Programme Grant BRIGHTLIGHT. LF/RT are joint CI on new proposal
3. Smith L, Glaser AW, Peckham D, Greenwood DC, Feltbower RG. Respiratory morbidity in young people surviving cancer: Population-based study of hospital admissions, treatment-related risk factors and subsequent mortality. Int J Cancer. 2019;145(1):20-28.	First comprehensive, population-based assessment of the burden of respiratory morbidity among long-term CTYA cancer survivors within secondary care.	Discussed and developed within subgroup in 2019.

4. Online information needs of young people with cancer Lea S, Martins A, Morgan S, Cargill J, Taylor RM, Fern LA. Health care professional perceptions of online information and support for young people with cancer in the United Kingdom. Adolesc Health Med Ther. 2019;10:103-16	Contractual agreement between Macmillan and TYAC to transfer responsibility and update of online information for young people ad to be hosted on TYAC website	Group members (RT,LF,SM) submitted funding application to Teenage Cancer Trust, conducted study, published.
5. Late effects and survivorship Smith L, Glaser AW, Greenwood DC, Feltbower RG. Cumulative burden of subsequent neoplasms, cardiovascular and respiratory morbidity in young people surviving cancer. Cancer Epidemiol. 2020;66:101711.	First comprehensive, population-based assessment of the total burden of late effects among long-term CTYA cancer survivors within secondary care.	Discussed and developed with subgroup in 2019.

Group involvement with NICE appraisals

However extensive involvement in NHS England Service Specification in relation to improving recruitment to clinical trials.