Monograph:
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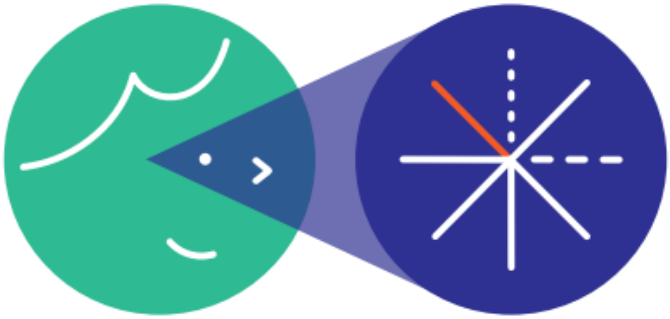

Social Transitions And Reintegration Support

S.T.A.R.S.

Social Integration After a Cancer Diagnosis

Chief Investigator:

Prof Dan Stark

University of Leeds

Supported by:

The Economic & Social Research Council (ESRC)

Sponsored by:

University of Leeds

Protocol version 3.4/01.04.2022

IRAS Study ID: 281857

Contents

PROTOCOL VERSIONS

Version Stage	Versions No	Version Date	Protocol updated & finalised by;	Appendix No detail the reason(s) for the protocol update
Approved	3	12.08.2020	Luke Hughes Oana Lindner	
Substantial amendment	3.1	14.01.2021	Oana Lindner	See Amendment tool
Non-substantial amendment	3.2	15.06.2021	Oana Lindner	See Amendment tool
Substantial amendment	3.3	16.09.2021	Oana Lindner	See Amendment tool
Non-substantial amendment	3.4	01.04.2022	Oana Lindner	See Amendment tool

STUDY SUMMARY

Identifiers	
IRAS Number	281857
REC Reference No	20/PR/0428
Other research reference number(s) (if applicable)	NIHR CRN ID: 46876 Sponsor reference number: MO20/135554 EDGE ID: 135554
Full (Scientific) title	Social Integration After a Cancer Diagnosis in Teenagers and Young Adults
Project Working title	S.T.A.R.S. - Social Integration After a Cancer Diagnosis
Health condition(s) or problem(s) studied	Cancer
Study Type i.e. Cohort etc	Mixed methods observational study combining a longitudinal prospective quantitative component with an embedded qualitative component.
Target sample size	528
STUDY TIMELINES	
Study Duration/length	24 months
Expected Start Date	01.03.2021
End of Study definition and anticipated date	13.06.2023
Key Study milestones	Sponsor submission; IRAS submission; PPIE consultations; Recruitment to Cohort 1 and 2 opens; Quantitative data collection at consent; Quantitative data collection at 6-month follow up; Interview administration; Quantitative data analyses; Qualitative data analyses; PPIE workshops (intermittent); Dissemination.
FUNDING & Other	
Funding	Economic and Social Research Committee
Other support	N/A
STORAGE of SAMPLES (if applicable)	
Human tissue samples	N/A
Data collected / Storage	Questionnaires online or paper plus interviews by telephone or videochat NHS Computers & locked document folders in restricted-access areas; University Computers & locked document folders in restricted access areas
KEY STUDY CONTACTS	
Chief Investigator	Professor Dan Stark MB BChir, MA, PhD, FRCP Email: D.P.Stark@leeds.ac.uk

KEY ROLES AND RESPONSIBILITIES

SPONSOR: The sponsor is responsible for ensuring before a study begins that arrangements are in place for the team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also has to be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATOR: The person who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether or not he/she is an investigator at any particular site. The CI role is to complete and to ensure that all relevant regulatory approvals are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards. The CI is responsible for submission of annual reports as required. The CI will notify the Research Ethics Committee (REC) of the end of the study, including the reasons for the premature termination. Within one year after the end of study, the CI will submit a final report with the results, including any publications/abstracts to the REC.

PRINCIPLE INVESTIGATOR (PI): Individually or as leader of the researchers at a site; ensuring that the study is conducted as per the approved study protocol, and report/notify the relevant parties – this includes the CI of any breaches or incidents related to the study.

RESEARCHER: Refers to the research/study team members based at the University of Leeds/University College London Hospitals NHS Foundation Trust funded to conduct the study.

DATA MANAGER: The Data Manager will undertake the database design, management, and database extractions. They will assist in data cleaning and organisation; ensure database coding and security, commensurate with the data management plan.

KEY WORDS

Cancer, Teenagers and Young Adults, Social Integration, Subjective wellbeing, Quality of life, Psycho-social factors, Education, Work, Social networks.

LIST OF ABBREVIATIONS

AE	Adverse Event
AR	Adverse Reaction
CI	Chief Investigator
CPQ	Close Person's Questionnaire
CRF	Case Report Form
EPR	Electronic Patient Records
EQ-5D	Standardised instrument for measuring health status
ESRC	Economic and Social Research Council
ICF	Informed Consent Form
HADS	Hospital Anxiety and Depression Scale
IPQ	Illness Perceptions Questionnaire
LTHT	Leeds Teaching Hospitals NHS Trust
NIHR	National Institute of Health Research
PCOR	Patient Centred Outcomes Research Group
PI	Principle Investigator
PIS	Participant Information Sheet
PPM	Patient Pathway Manager (EPR used in LTHT)
PRO	Patient Reported Outcomes
QTool	Flexible web-service linking the online surveys with the NHS-based EPR
REC	Research Ethics Committee
SAR	Serious Adverse Reaction
SAE	Serious Adverse Event
SOP	Standard Operating Procedure
SI	Social Integration
SSI	Site Specific Information
TCT	Teenage Cancer Trust
UCLH	University College London Hospitals NHS Trust
TYA	Teenagers and Young Adults
YAG	Youth Advisory Group

1 GENERAL INFORMATION

1.1 Purpose of the protocol

This focus of this protocol is a one of three studies (henceforth referred to as "Study 3"), involving novel data collection. It is one of the three linked studies of a larger research project, which aims to describe the trajectories of social integration (SI) in teenagers and young adults (TYA) following a cancer diagnosis.

Study 3, described in this protocol, is an observational mixed methods study exploring the psycho-social factors, patient-reported outcomes (PROs) and any additional emerging factors enabling or disabling the SI trajectories in this population. **Participants will be TYAs aged 16 to 39 who are either 10 weeks to 6 months post-diagnosis (Cohort 1) or 3-5 years post-treatment (Cohort 2), under the care of Leeds Teaching Hospitals Trust or University College London Hospitals.** Data collection will involve two survey waves and a semi-structured interview, complementing and enriching the findings of the secondary data analyses performed in the other two studies of the research project.

1.2 Protocol use

This document describes the details and procedures of Study 3. For clarity, below we offer an overview of the research project, before offering details related to the design and procedures of Study 3.

1.3 Protocol authorisations and amendments

The final protocol and any amendments will be authorised by the Chief Investigator (Professor Dan Stark) and sponsor (University of Leeds). Any corrections/amendments will be circulated to co-investigators. For any communications or queries please contact the study co-ordinator, Dr Oana Lindner on o.c.lindner@leeds.ac.uk or the study Chief Investigator, Prof. Dan Stark on d.p.stark@leeds.ac.uk.

1.4 Compliance

All aspects of the study will be undertaken in accordance with the MRC Good Research Practice guidelines, Good Clinical Practice (GCP) guidelines and the Data Protection Act (2018).

1.5 Sponsor

The University of Leeds will act as Sponsor for research involving the NHS, as defined in the UK Policy Framework for Health and Social Care Research (2017), where the Chief investigator is a substantive employee.

1.6 Funder

This study is funded by the Economic and Social Research Council (ESRC, ES/S00565X/1).

2 MAIN CONTACTS

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3 PROJECT OVERVIEW

3.1 Background

In 2015, the Independent Cancer Taskforce identified the need to moderate the long-term consequences of cancer. Psychological and social needs have been emphasised as a priority by the James Lind Alliance priority setting exercise (Aldiss et al., 2018). Given advances in oncological care, a large population of cancer patients are now living with and beyond their cancer and its treatment. According to recent statistics a growing number of these patients are thought to be TYAs aged 16 to 39. Our understanding of adolescence and young adulthood is informed by Arnett's (2004) definition of emerging adulthood which incorporates the ages of the early 20s-30s, as well as keeping international approaches to care in perspective (Teenage Cancer Trust, 2016). Therefore, for the purpose of this research we define the category of TYA as including people between 16-39.

While TYA five-year survival rates increased in recent years and now approach 90% (Stark et al, 2015) across diagnoses, survival rates are not an indication of subjective wellbeing, life satisfaction or quality, and do not account for the impact of the cancer diagnosis and its treatment on physical, psychological, social outcomes. Late effects may be caused by both cancer and its treatment. Such effects may span across physical effects (long-term consequences of treatment and second cancers), psychological (emotional and cognitive), and social problems (employment, education, and social networks) and be inter-related (NCI, 2019).

A diagnosis of cancer represents a 'critical situation' which may result in an experience called 'biographical disruption' (Bury, 1982). It can be seen as a disturbance to life trajectory, which may cause confusion, may impede progress and lead to changes in goals, aspirations and the strategies to reach these (Tembo, 2017). Hence, a cancer diagnosis may disrupt processes related to gaining independence and forming an identity, interrupting or changing the development of a personal biography, or psycho-social trajectory, and as a result changing one's expectations of future life (for better or for worse). This may, in turn, lead to a change in subjective wellbeing (SWB) or quality of life (QoL).

The period between 16 and 39 years old is defined as one of 'emerging adulthood' (Arnett, 2004), characterized by multiple developmental transitions and milestones (Grinyer, 2007), especially in terms of their Social Integration (SI). Consequently, across the entire research project and within Study 3, we refer to SI as outcomes related to: (1) employment (quantitative markers such as income, and qualitative markers such as satisfaction) (Parsons et al., 2012; Heinesen et al., 2017); (2) education (quantitative markers such as level of education and qualitative markers such as satisfaction) (Lancashire et al., 2010; Pini et al, 2012); (3) social networks (quantity and quality of perceived social support online and offline) (Mathieson & Stam, 1995; Grinyer, 2007; Podmore et al., 2009; Hodge & Runswick-Cole, 2013); (4) and subjective wellbeing (i.e. satisfaction with key life domains such as health, family, income, social relationships, leisure time, work and sex life) (Diener et al., 1999; Dolan & Metcalfe, 2012).

During this period of 'emerging adulthood', 'critical situations' (Bury, 1982) such as a cancer diagnosis, may increase vulnerability to disrupted work, education, or social networks trajectories for TYAs. Hence, for TYAs, the process of SI following a 'critical situation' (Bury, 1982) emerges at an intersection of internal and external determinants which are not yet fully

understood. SI with peer groups, defining one's identity and independence are normatively considered key milestones for this demographic (Warner et al, 2016). Unmet psychosocial needs, including feeling different and distanced from peers, may contribute to poorer outcomes (such as lower SWB/QoL) compared to children and older adults (Pritchard et al, 2011). Understandably, life after cancer brings with it many new challenges, particularly for TYAs whose experience of cancer occurs at this uniquely vulnerable time of their psychological and social development. Hence, within our project, we define TYAs' SI trajectory as the changes in goals and associated strategies needed to establish a new or alternate psychological and social trajectory or re-defining it, consistent to previous or new goals. Here, SI is not just the opposite of social isolation and exclusion (Seeman, 1996; Wilkinson & Marmot, 2003) but a dynamic process of establishing a new/alternative life trajectory and achieving a new sense of personal and social 'normality' following a biographic disruption (Bury, 1982; Williams, 2000; Grinyer, 2007). Before we can understand how best to support young people's SI following a cancer diagnosis, we must first understand which factors contribute (either together or independently) to enable or disable TYAs' SI trajectories more generally.

3.2 Project structure

The research project explores SI outcomes over time through 3 interconnected studies (see Figure 1).

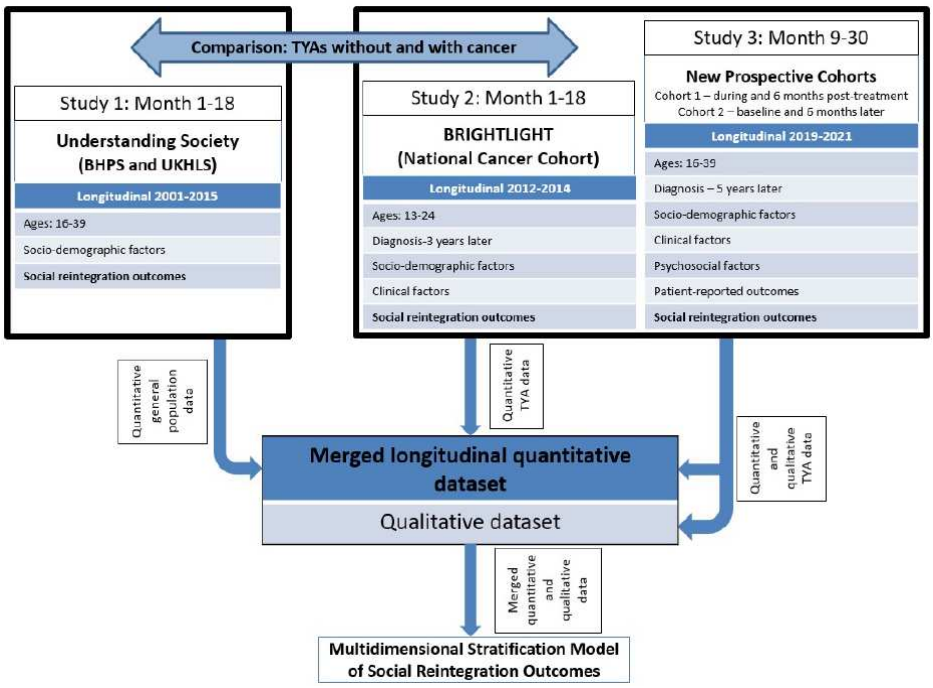

Figure 1. Structure of Project data sources and analyses

Studies 1 and 2 explore SI trajectories through secondary data analyses of existing datasets. Study 1 uses secondary data from the ESRC-funded UK Household Longitudinal Study (Understanding Society) to identify the demographic factors influencing SI trajectories in the general population. Apart from offering us insight into the socio-demographic stratification of SI outcomes, this part of the project will provide a 'counterfactual' (i.e. a matched comparison group) for the information we collect from people diagnosed with cancer within Studies 2 and 3.

Study 2 draws upon secondary data from the NIHR-funded BRIGHLIGHT dataset to define key clinical factors that affect SI for people diagnosed with cancer. This dataset will help us define the potential cancer-related factors influencing the trajectories of SI outcomes described above in people aged 16 to 24 from 10 weeks to 3 years post diagnosis.

Study 3, which involves a novel quantitative and qualitative data collection, is the focus of this protocol, described in depth below.

On completion these three studies will provide a Multidimensional Stratification Model of Social Integration Outcomes. We will explore with patients and healthcare professionals how the model could be best integrated within current NHS practices in order to reduce inequality of opportunities for TYAs following a cancer diagnosis.

4 STUDY 3

4.1 Impact of Cancer on TYAs

4.1.1 Work and Education

In terms of work and education, a cancer diagnosis will heavily impact TYAs' ability to participate and to follow opportunities, meaning they may miss out on key developmental milestones and feel they have fallen behind their peers (Taylor et al, 2013). They are likely to experience widespread absence from school, which may affect their educational momentum and their ability to sit exams, as well as the daunting possibility of having to repeat courses in an entirely new cohort, leading in a loss of previous social support networks (Goodall et al., 2012). Similarly, they may miss out on educational progression that they had planned, disrupting their expected trajectory, or have key members of their social support networks leave to attend university (Grinyer, 2007, Goodall et al., 2012). Disruptions to education may lead to a change in their career aspirations, or what they believe is achievable. Cancer-related physical disabilities may also limit or entirely change their career prospects (Tai et al., 2012) while chronic or late effects from cancer and its treatment may impact their ability to fulfil certain roles and obligations in the work and/or social environment (Parsons et al, 2012). Research shows TYAs are likely to express feelings of restriction or discrimination in the work place due to limitations from chronic or late effects of cancer treatment (Jacobson, Biddle , Daeschner et al, 1995, Dolgin , Somer , Buchvald et al, 1999 Parsons et al , 2012). Parson et al (2012) found that of those who returned to education or work 15-35 months after diagnosis, 50% reported issues with their reintegration into these settings. TYAs describe a sense of loss due to poorer contact with their peers and less opportunities to participate in activities they consider to be normative for their age group. This, may in turn, contribute to feelings of loneliness and isolation particularly with regards to their education or their roles in the workplace (Zebrack, 2011, Smith et al, 2013, Taylor et al, 2013).

4.1.2 Social Development

Cancer often has a significant effect on the social circles of TYAs. TYAs are known to spend a large amount of time with their primary caregivers during treatment and may become dependent on them. This process takes priority over forging and consolidating new friendships with their peers (Chesler & Barbarin, 1987). Social development may also be impacted by the disintegration of previous friendships due to the presence of cancer, and an apprehension about bothering friends or making new friends (Chesler, Wiegers and Lather,

1992). Mackie et al. (2000) reported that young people struggled with forming new close relationships even after treatment had ended, and often continue to be more dependent on family members; such a phenomenon may perhaps be related to changes in social networks having taken place following their diagnosis and/or additional challenges in their functioning following their treatment. It may also reflect internalised stigma related to their abilities – whether physical, emotional, or otherwise (Kent et al, 2012, Smith et al, 2013).

Likewise, a cancer diagnosis is also shown to impact romantic relationships, sexual identity and sexual expression, with TYAs potentially missing out on many of the friendship and romantic relationships their peers would experience (Thaler-Demers, 2001). TYAs have frequently expressed dissatisfaction with their sex lives post treatment, struggling with poorer body image, intimacy, and fears around disclosing an experience of cancer to a potential partner (Tahler-Demers, 2001; Carpentier & Fortenberry, 2010). These experiences can challenge TYAs' self-efficacy in developing new close relationships at a time when this is most important. Concerns over fertility and its impact on future plans for relationships, family and lifestyle are also common threads among this cohort (Zebrack et al, 2004, Chapple et al, 2007). These difficulties can impede emerging psychosexual development and identity and influence their ability to socialise and forge intimate/romantic connections, making social integration more arduous.

Research suggests that TYAs are likely to turn to using social media to facilitate their social lives (Teenage Cancer Trust, 2016). Social media has been shown to be useful for maintaining friendships over distance created by long periods of hospitalisation, and for collectively providing a space to inform, educate and connect with friends (Boyd, 2014). Some young people may feel more able to be themselves online (Livingstone et al, 2011), perhaps offering some distance from their cancer identity and/or helping them connect with people with similar experiences. How friendships develop offline and online and in what circumstances they may offer a source of support or not for TYAs with and without cancer is still debated.

4.1.3 Subjective Wellbeing

Worry or reluctance around socialising with peers has been observed following treatment (Seitz et al, 2010). Symptoms of stress associated with the trauma of diagnosis and treatment (e.g. sadness, fear, low self-esteem) have been shown to affect up to 44% of a sampled TYA population (Seitz et al, 2010, Kwak et al, 2013) largely in regards to a fear of disease recurrence (Grinyer, 2007). On the other hand, TYAs have also reported positive outcomes relating to their experiences of disease. This has been termed 'post-traumatic growth', an adaptive change in focus, goals, or coping mechanisms which can inform a person's word view, can serve to guide the development of new/alternative trajectories, and may contribute to enrichening personal relationships. Hence, for some, the experience of the cancer diagnosis as a 'critical situation' may also have a positive impact on how young people see both themselves, others, and the world around them (Janoff-Bulman, 1992, Cohen et al, 1998, Tedeschi, Park & Calhoun, 1998). For example, Parry and Chesler (2005) found that childhood experiences of cancer had positive effects on some individuals, particularly on their psychological maturity, empathetic abilities, values, sense of inner strength, and spiritual growth. Whether such changes have a positive or negative influence on interactions with their peers and how they view themselves, their futures, and general wellbeing is still debated.

The case remains, however, that not all young experience positive outcomes following their diagnosis (Luthor, Cicchetti & Becker, 2000) and most still experience negative outcomes such as ongoing physical, psychological, economic, and social concerns (Zebrack & Chesler, 2001). Although many TYAs have a good prognosis, a cancer diagnosis is still a stressful, live changing event with long-term effects on a persons' life and wellbeing (Kyngas et al., 2001). While Mattsson et al (2007) found that TYAs often report a mixture of positive and negative consequences, Carpentier et al (2011) found that even though awareness of these positive aspects may be present, TYAs continue to feel isolated from their peers as a result of disparate levels of maturity and life experiences. Why some people may experience post-traumatic growth or not may potentially be shaped by factors present before the diagnosis itself, hence knowledge on their 'baseline' is necessary.

We do not fully understand what factors facilitate or inhibit positive and negative experiences in various people. However, we hypothesise that first, demographic factors may offer some insight into potentially vulnerable groups, which we will investigate via Understanding Society in Study 1. Second, factors related to the type of diagnosis, type and length of treatment will be investigated within Studies 2 and 3. Finally, psycho-social and any other factors potentially not yet accounted in the literature will be sought and explored in Study 3.

4.2 Summary

To date, SI outcomes and related potential inequalities of opportunity in TYAs after a cancer diagnosis have only been estimated or hypothesised based on small samples. Despite evidence of poor psychosocial, cognitive, and emotional outcomes in TYA cancer patients, we do not understand to what extent and in whom these outcomes may be poorer compared to similar peers.

The experience of a cancer diagnosis and treatment can change a person's life view and trajectory, for better or for worse, or more likely both. Cancer is a profoundly social, personal and subjective experience (Davieson et al 2000). What leads some to struggle and others to grow is therefore a complex active process of renegotiation of not just the individual's social and world view but their subjective experiences of their life elements before, during, and after their treatment. Here we will attempt to understand what sort of groups need specific type of support to readjust their trajectories to fit with their aspirations and goals identified over time.

Furthermore, we cannot know to what extent any of these outcomes may influence (or not) TYAs' developmental trajectories after their diagnosis (Fern et al., 2013). Little is known about how initial resources and expectations of education, employment, or social networks may influence their experiences through diagnosis and treatment, in turn further shaping their SI expectations and outcomes after treatment. This is a critical area for action and while there is evidence that SI is linked QoL, many other aspects could also contribute, including ongoing symptoms, fear of recurrence, satisfaction with employment, physical appearance concerns, etc. (Seitz et al, 2010). Hence, to enable interventions for those populations who may need it most, we first need to understand the factors that may contribute to enabling or disabling TYAs' SI trajectories.

Study 3 aims to explore the above factors which may influence TYA SI trajectories over and above demographic and clinical factors established in Studies 1 and 2. The study will focus on people aged 16 to 39 who are 10 weeks to 6 months post-diagnosis (Cohort 1) and 3-5 years post-treatment, extending the age and time span since diagnosis observed in BRIGHTLIGHT (2015). We explore a range of psychological, social factors and patient-reported outcomes (PROs) in addition to those measured in BRIGHTLIGHT and Understanding Society (e.g. extraversion, self-efficacy, quality of social networks). Later, by integrating the findings of the two secondary data analyses with the findings of Study 3, we will be able to identify the main factors impacting on SI after a cancer diagnosis to include them in future psychosocial support packages.

A secondary aim is to understand the intersection of the impact of a cancer diagnosis and the novel CORONAVIRUS (COVID-19) outbreak on the same SI integration outcomes for young people. This objective will be met by our data collection taking place following the COVID-19 outbreak and comparing our findings to new Understanding Society waves (2019) as a post-COVID-19 counterfactual in the general population and with the pre-COVID-19 Understanding Society and BRIGHTLIGHT datasets.

5 OBJECTIVES

5.1 Primary Objective

The primary objective of this study is to identify SI trajectories and the potential influence of psychosocial and other emerging factors amongst young people diagnosed with cancer. We expect (Hypothesis 3, Study 3) SI trajectories for people with specific demographic backgrounds, and specific cancer clinical profiles (as defined in Study 1 and 2)[1] to vary to different proportions due to explanatory factors such as fatigue, emotional distress, illness perceptions, subjective cognitive difficulties, perceived social support, physical appearance, post-traumatic growth, and personality factors. These factors will be explored through our quantitative work, allowing for the emergence of new factors through our qualitative work.

5.2 Secondary Objectives

Our project design, including data collected in Study 3 will contribute to differentiating between the effects of cancer versus COVID-19 on TYAs' outcomes over time.

6 METHODS

6.1 Study design

Study 3 is a mixed methods observational study combining longitudinal prospective quantitative data collection with an embedded iterative qualitative component.

6.2 Setting

[1] Hypotheses 1 and 2 relate to the Studies 1 and 2 of the project. H1 (Study 1): We expect people from different demographic backgrounds to have different SI trajectories over time. H2 (Study 2): We expect people with cancer diagnoses to have different trajectories over time, after accounting for the demographic factors identified in Study 1.

Two cohorts of participants (see Figure 2) will be sampled across two centres (Leeds and London). The recruitment of TYAs aged 16-25 will take place via TYA inpatient wards and outpatient clinics; the recruitment of TYAs aged 26-39 will take place via specialist adult inpatient wards and outpatient clinics. In both London and Leeds, there are approximately 250 new referrals per annum of TYA aged 16-24 and approximately 500 aged 25-39.

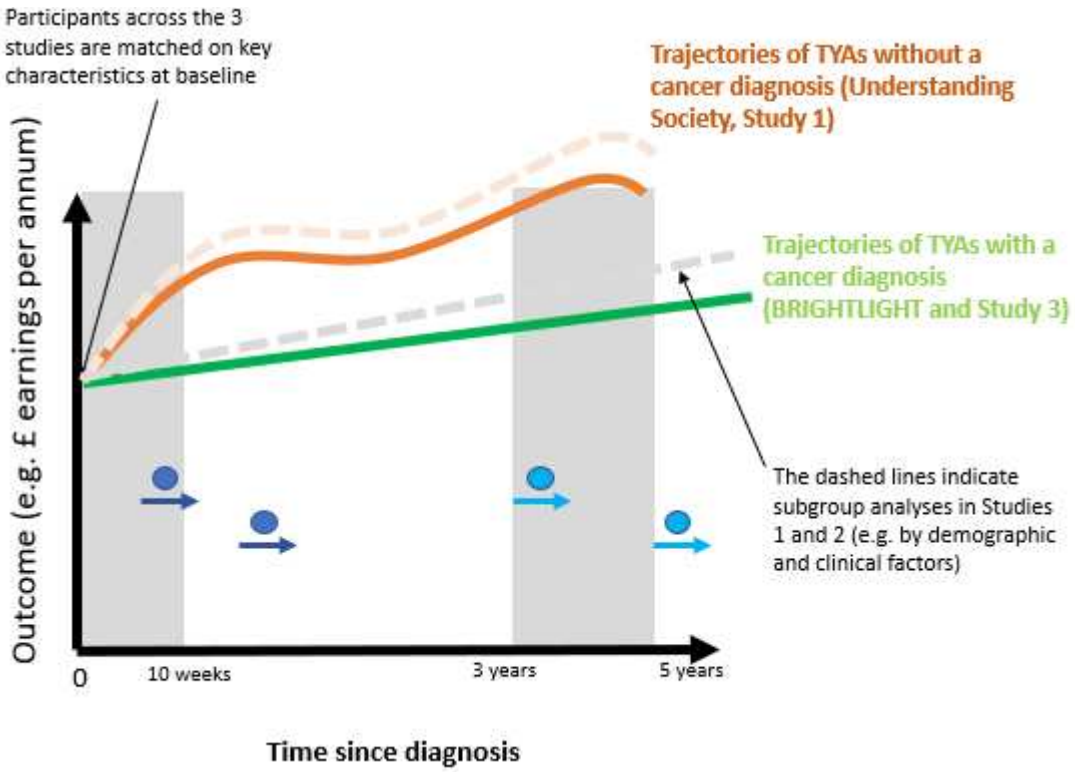

Figure 2. Cohort Structure. Legend: Dark blue arrow (→) - **Cohort 1,** Survey Wave 1: 10wks to 6months post-diagnosis and Wave 2: 6 months after Wave 1. N=264. Light blue arrow (→) – Cohort 2, Survey Wave 1: 3 to 5 years post-treatment and Wave 2: 6 months after Wave 1. N=264. Circles: Interview subsamples within Cohort 1 (interviews conducted up to 3 weeks after Wave 1 OR 6-8 weeks after Wave 2) and Cohort 2 (interviews conducted up to 6-8 weeks after either Wave).

6.3 Participants

6.3.1 Sample size – Quantitative sub-study

The target sample size for Study 3 is N= 528, divided equally across Leeds and London (N=264, per site). In each location we will aim to recruit an equal number of participants (N=132) to Cohorts 1 and 2, respectively.

A priori power calculation for Study 3 was pursued using the most recently published Office of National Statistics cancer registry (ONS, 2017) and Cancer Research UK (CRUK, 2019) information on incidence and prevalence of TYA cancers, by disease groups outlined in O'Hara et al. (2015).

For Cohort 1, we used information related to incident cases for 15-39 year olds. Figures from the ONS are released as cases per 100,000 people, which we used to estimate incidence for each cancer type. Population figures for the UK were obtained from the 2017 ONS mid-year estimate. The total incidence, broken down by cancer types were calculated by multiplying the rate of incidence/100,000 by the total population of the UK/100,000. This was

subsequently broken down to find the total incidence rate in London and West Yorkshire, to reflect figures in the areas of interest for this study. Exact figures for the population of London and West Yorkshire were obtained from the 2017 ONS mid-year estimate.

For Cohort 2, data for the 5-year survival rate of cancers in TYA were extracted from the ONS data on cancer survival in England, between 2013-2017, or from O'Hara (2015) where ONS data lacked detail. Here 5-year survival for the TYA population after 5 years is calculated as survival rate/100*incidence.

A fixed-effects ANOVA with 2 groups at 80% power to detect smallest effect size with 0.05 significance for 8 outcomes was conducted to identify sample size **N** per cohort. **N** was multiplied by 2 to find the total number of participants required in both cohorts. The figure for both cohorts combined was multiplied by 1.5 to account for a 50% attrition rate between Survey waves, which resulted our target sample per site of **N=264**.

Hence, we will aim to recruit 264 participants per centre, divided between Cohorts 1 and Cohorts 2. This will include the following ICD codes related to malignant neoplasms and carcinomas prevalent in our target age group (C00-C97, D00-D09, and D37-D48).

Throughout recruitment, progress for each group will be monitored in real time at each weekly and quarterly team meeting and may be adjusted per diagnosis and centre based on participant availability. These recruitment numbers will be suitable both for determining the impact of a cancer diagnosis on SI outcomes over time, and for our secondary objective of differentiating between the effects of cancer and COVID-19 on the same outcomes.

6.3.2 Sampling strategy - Qualitative sub-study

We expect to run the interviews with 100 participants, divided across 4 groups, as guided by advice on interview saturation (Francis et al., 2010). The groups are stratified by location (equal number of participants between Leeds and London), cohort (equal number in Cohorts 1 and 2), age groups (16-24 and 25-39), and time points of the survey (half following Wave 1 and half following Wave 2). If needed and necessary, our current sampling strategy may be updated if other relevant subgroups emerge from the analyses in Studies 1 and 2. Any such updates will be included in the substantial amendment pertaining to the qualitative sub-study. Each participant will only sit one interview throughout the project, hence the participants recruited in Waves 1 and 2 will differ. Figure 3 below depicts the current proposed sampling strategy for the qualitative study, with the note that any changes to our targets will be included in a subsequent amendment to this protocol:

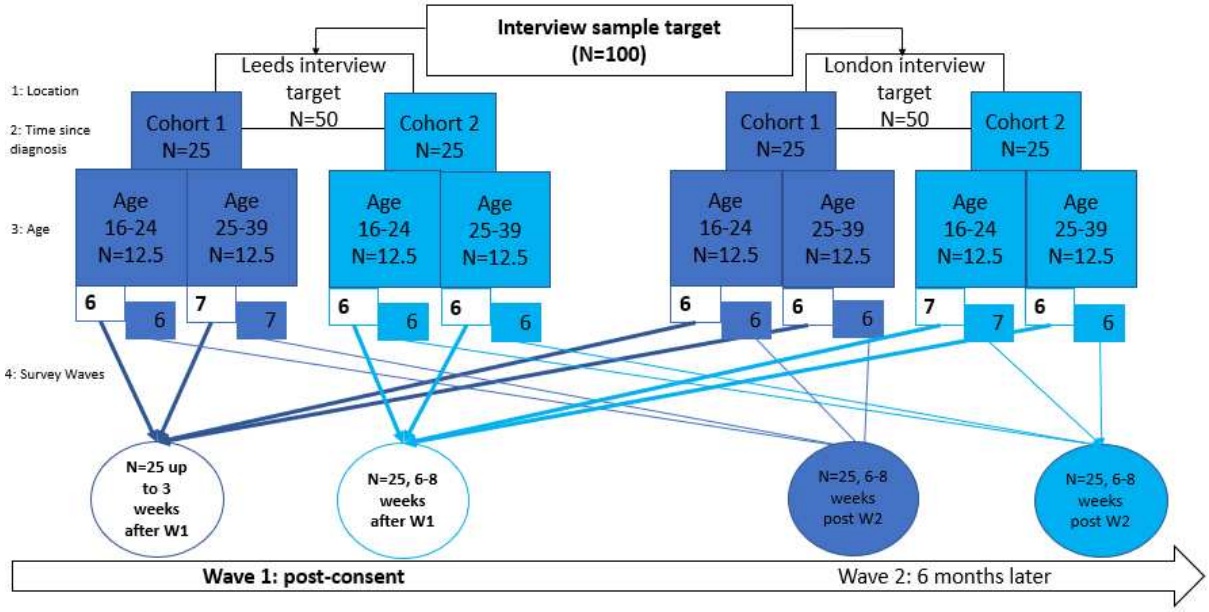

Figure 3. Sampling strategy for qualitative interviews, depicting the target number of participants across locations, time since diagnosis, age, and survey waves.

6.4 Eligibility

6.4.1 Inclusion criteria

Cohort 1:

- Aged between 16-39 at study entry
- Within 10 weeks to 6 months of their diagnosis of their most recent primary cancer
- Patients who have previously had a different cancer and have been diagnosed with a second malignant neoplasm within the last 6 months are eligible
- Treated in regional cancer centres in Leeds and London
- Able and willing to give informed consent
- Able to read and understand English.

Cohort 2:

- Aged between 16-39 at study entry
- Treatment for cancer ended 3-5 years prior to date of study entry
- Treated in regional cancer centres in Leeds and London
- Able and willing to give informed consent
- Able to read and understand English.

6.4.2 Exclusion criteria

Cohort 1:

- A member of our Youth Advisory Group
- Private patients in an NHS setting
- Low to no level of English comprehension, even when supported
- Patients with a medical diagnosis which is likely to transition to End of Life care before the second time point of the study (i.e. within 6 months of study entry)

- Young person is receiving a custodial sentence
- ICD 10 codes outside of ICD 10 CM C00-D48 (ICD 10 CM, 2020)

Cohort 2:

- A member of our Youth Advisory Group
- Patients being treated under End of Life care
- Private patients in an NHS setting
- Patients with a medical diagnosis which is likely to transition to End of Life care before the second time point of the study
- Young person is receiving a custodial sentence
- ICD 10 codes outside of ICD 10 CM C00-D48 (ICD 10 CM, 2020).

6.5 Participant recruitment

6.5.1 Identification

Patients will be recruited on the premises of the participating NHS sites (Leeds Teaching Hospitals NHS Trust and University College London Hospitals), via inpatient and outpatient/ambulatory care (Cohort 1 and Cohort 2).

Prior to the start of recruitment, the study team in each participating center will send the clinical teams involved in the care of TYAs a letter/email introducing the study (Appendix 1), requesting permission to recruit potential participants. When participants in these centers self-refer after seeing posters or leaflets in the units/clinics where we are recruiting (if this procedure is applicable to the particular study site), the clinical team will be notified of their interest (Appendix 1) by the local study team.

Eligible patients will be identified by screening of the clinic or day case lists by clinical teams directly involved in their care. The most suitable person (either oncologist, doctor, nurse, youth support coordinator, clinical team member or multidisciplinary team (MDT) coordinator) will be identified to perform the screening of the clinic lists. The screening process will be supported by the use of the Study eligibility checklist (CRF01, Appendix 9), when the study number will also be assigned in the format: 1.001.DD.MM.YY.SJUH.1, whereby the first digit is the Cohort number (1 or 2), the following 3 digits are the Participant number (starting with 001), the next six digits are the date when the potential participant was identified, the following 4 letters are the study site (either SJUH or UCLH) and the final number is the participant consent status (either 1 if they consented or 0 if they did not consent).

Patients in the qualitative sub-study will include patients who have already consented to the study in either cohort and agreed to be re-contacted. Participants not initially involved in the survey may be recruited for the qualitative sub-study via the same methods described above if saturation is not reached. Additional details of this latter process will be discussed and agreed with patient representatives and submitted for additional review, if needed.

Patients who are still under the care of their treatment team but no longer attend face-to-face appointments will also be eligible. We will work with clinical teams (in London and Leeds) to send a Study invitation email/letter with a copy of the survey (Appendix 1) to eligible patients

to explore interest. If interested, patients can opt into the study by either (1) completing the survey and consent form and sending it back to the study team; or (2) contact the study team directly via the contact details offered in the letter or (3) can request a call/email back by offering their contact details to the study team in the particular NHS site. Clinical teams in Leeds and London will provide the local study team with the necessary contact details (either in person or via NHS email) if the patient agrees they would like to be contacted about the study.

6.5.2 Approach

Eligible patients will be identified by an appropriate member of the clinical team in the local NHS trust during routine clinic appointments (whether it's in person or remote via letter/phone call).

Recruitment during face-to-face appointments: Members of the clinical team will identify eligible participants for either cohort, briefly describe the scope of the study and offer a Participant Information Sheet (PIS, Appendix 2). If the patient is interested in the study, one of the members of the clinical treatment team will introduce them to a member of the study team while the patient is in clinic. The member of the study team will give patients the consent form (Appendix 3) and survey (Appendix 7), offer details on the study and answer any questions.

Recruitment during remote appointments: Patients who are recruited remotely will receive the same PIS as well as the survey (Appendix 7) and consent form (Appendix 3) via an introductory letter/email from a member of the clinical team after their remote consultation. This will enable participants to make a fully informed decision as to whether they would like to take part, by having seen the survey they are asked to complete. If interested, patients can return the completed survey and consent form to the study team using a pre-paid envelope; alternatively, they can contact the study team directly to request a call back, discuss the study further and, if preferred, request an online version of the survey. Clinical team members will provide the study team with the necessary contact details for patients to be contacted by the study team if the patient prefers and agrees to a call-back.

Alternatively, potential participants in the specified NHS sites can contact the local study team directly. Posters/leaflets with QR codes (Appendix 5) can be made available in clinics, depending on local site regulations, allowing patients to also self-refer to the study.

6.5.3 Informed consent

All participants taking part in this study will have to provide informed written consent, whether this is done on hardcopy or electronically. As the age range for this study is 16-39, patients will be able to self-consent to the study before completing the survey. To ensure inclusivity within our centers we will be able to provide participant information sheets in easy read versions to those who would like one and other accessible formats (i.e. Braille) will be made available upon request (see Appendix 2, PIS easy-read versions).

The principal investigator or any other qualified member of the study team with an up-to-date Good Clinical Practice Training (GCP) and an NHS honorary contract will be able to take informed consent. The right of the patient to refuse participation without giving reasons will be respected. If a patient prefers more time to consider their participation, they will be able to

take the information home, discuss it with family, carers or peers, and inform the researcher at a later date (over the phone/video chat/email) or during their next hospital visit as applicable. For patients who are eligible and approached but decline participation, participating centers will be required to keep a record of these patients; anonymised information will be collected, including reason for declining participation (if volunteered). This information, as well as type and process of recruitment and study completion will be monitored throughout the study by the study team at each NHS site using a Recruitment monitoring form (Appendix 10).

Consent procedure: After reading the PIS (Appendix 2) and having had the opportunity to ask questions, patients will provide written informed consent, either on paper (Appendix 3) or electronically, agreeing to the same statements.

If participants complete the survey on paper on the NHS premises or via post, consent will be obtained on paper forms (Appendix 3). Easy read (see Appendix 2) and additional accessibility consent forms will be made available upon request to improve the inclusivity of our recruitment.

If participants prefer to complete the survey online via QTool or any other University of Leeds and NHS-approved online questionnaire system from home, consent will be obtained via said software, under appropriate GDPR and Data protection regulations. In the latter circumstance, patient consent will be taken in writing using the online consent procedure within the online questionnaire, QTool which was developed in accordance with HRA & MHRA Guidance (2018) Joint Statement on seeking consent by electronic methods. We developed a bespoke online consent form (see Appendix 3, Online consent form). Once participants request the use of the online questionnaire, the researcher logs onto the system and issues a unique username and password for each participant. The patient then uses these to log onto the system (e.g. QTool) tocomplete the online consent form and survey. The system automatically enters the unique username and date stamp onto the online form, alongside the participants' answers to each statement on the consent form. The consent to each statement will be stored in the NHS site file, and if requested, a copy given to the patient and a copy filed or uploaded to the patient hospital records.

After completing Wave 1 of the Survey, before contacting a participant for either the Interview or Wave 2, **the patients' health status will first be confirmed by their clinical care teams**. In the event of a relapse, patients will be withdrawn from the quantitative study but will still be able to participate in the interview, at a later date, should they wish.

During the consent procedure, we will record the contact details of a named person (such as a caregiver) who has ongoing contact with the participant, should we lose contact with them between the time of administering Wave 1 and Wave 2 questionnaire or interview. This person will only be contacted once the clinical team have confirmed their health status and if we have failed to make contact with the young person or their next-of-kin within a month of when the Wave 2 questionnaire/interview are due. This strategy will be useful for this age group as young people relatively frequently change their phone or email provider or addresses.

Information about the interview will be provided initially at the first contact, where participants can express their interest; a participant information sheet with an attached interview prompt (see Appendix 2 non-easy read PIS Interview, p.7) will be provided to all participants who initially expressed an interest 7 to 14 days week before the 3-weeks (Cohort 1 Wave 1) or 6-8 week (Cohorts 1 Wave 2; Cohort 2 both waves) interview windows. Verbal (audio-recorded) or written consent will be taken before beginning interviews. Consent for interviews (but not any other parts of the study) will also include a statement related to the sharing of patient contact information between London and Leeds using the secure NHS email, to ensure sufficient manpower for conducting audio-recorded interviews across the two sites. This procedure will be implemented only on a needs-basis if a team member from Leeds or London had to cover study team member on either of the sites. This procedure will not be used if an easy read consent form is used (as recorded on the Recruitment Monitoring form, Appendix 10).

Consent for the interview will be gained either using the paper/email version of the Interview consent form (with an easy read version in Appendix 2) or will be digitally recorded before the start of the interview by the study team member from one of the 2 sites.

In all these circumstances, paper/emailed/recorded versions of the consent form will be kept separately from the completed survey, digitally recorded interviews or their transcripts.

Participants will be informed (see Appendix 2, PIS) and will consent (see Appendix 3, Consent forms) that their General practitioner may be informed of their study participation by the Principal investigator at each study site using the localised information letter (Appendix 1).

6.5.4 Withdrawal

Participants can withdraw at any time from the Study without having to offer a reason. A reverse cool-off will be possible, should patients retroactively decide they no longer wish to participate in the study and/or if they wish their data was removed from the study.
Upon withdrawal, researchers will fill in the Withdrawal form (Appendix 11). Their data will be taken out of the study, as long as it is practicable (i.e. participants' link to their anonymised code is destroyed once the participant finishes their involvement in the study – see section 9.1, p.24), upon request from the participants or their caregivers, in the event they lose capacity to consent during the study timeline. We are expecting both passive (no reason given) and active withdrawals to take place.

7 DATA COLLECTION

7.1 Clinical information

As this study focuses on the impact of cancer on SI trajectories, obtaining some limited and relevant clinical information on our participants is important. Clinical information will be extracted from hospital records after the participant's explicit consent. The information will include their diagnosis, time since diagnosis, their type of treatment and time since treatment, and whether they are known to have any other long-lasting health conditions. This information will be obtained via their clinical team who, following informed consent, will support the study team in filling in the clinical case report form (Appendix 6) with the relevant

information. This information will be updated, as needed, at Wave 2 for both cohorts (see Appendix 6).

7.2 Quantitative data

Quantitative data will be collected using a bespoke Survey (Appendix 7). It contains validated questionnaires which have been extensively used in this population, and items derived from and extending prior large population surveys encompassed by Studies 1 and 2 (Understanding Society and BRIGHTLIGHT). Survey items have been harmonised with these previous studies to facilitate planned outcome comparisons on employment, education, and social relationships with Understanding Society (2019) and BRIGHTLIGHT (Taylor et al, 2015). Validated measures of PROs will be used, focussing upon current physical symptoms, fatigue, emotional distress, illness perceptions, subjective cognitive difficulties, perceived social support, and physical appearance, post-traumatic growth, personality factors (e.g. extraversion, self-efficacy) and SWB/QoL.

Both waves are divided into 6 modules capturing our outcomes of interest and factors known to be related to social outcomes. Wave 1 contains 150 questions, while Wave 2 contains 134 questions. The survey will be administered to participants once they consent to the study via a. online via QTool, b. on paper, c. on a tablet, or d. verbally. Wave 2 will be administered within 6 months following consent.

The 6 modules are organised as detailed in Table 1, below.

Module	**Content**
(1) Demographic module (N=6)	• First part of postcode plus first digit of second part (to allow for comparisons between area levels of deprivation) • Month and year of birth (to account for age ranges and groups) • Gender • Ethnicity • Current activity (i.e. whether employed, in education etc) • Marital status
(2) Physical health module (N=6)	• Potential ongoing chronic illnesses • Difficulties with daily activities (EQ-5D) *Details on the type and time since diagnosis, type and time since treatment, and ongoing conditions will be extracted with the support of the clinical teams from the electronic patient record (EHR).

(3) Education module (N=7)	• Highest qualifications obtained to date • Losses in educational time due to cancer diagnosis and/or treatment • Importance of education prior (only in Wave 1) and following their diagnosis (both Waves) • Their pre-diagnosis educational plans (only in Wave 1) • Current educational plans (both Waves) • Satisfaction with current educational/training provision. *If some questions are not applicable based on the information provided in Module 1 (see Current activity), participants will be able to skip some parts of this module.
(4) Work module (N=21)	• Current employment status (including options for 'in-work poverty') • Career plans prior to diagnosis (only in Wave 1) • Career plans currently (both Waves) • Annual/monthly income bracket • Satisfaction with earnings • Areas of importance in terms of career prior to their diagnosis (only in Wave 1) • Areas of importance in terms of career at present (both Waves) • Whether they felt they could share their diagnosis with employers and/or colleagues • Future employment plans • General satisfaction with work *If some questions are not applicable based on the information provided in Module 1 (see Current activity), participants will be able to skip some parts of this module.

(5) Social networks module (N=36)	• Current household composition (i.e. how many people are there in their households) • Quantity and quality of social relationships, both online and offline. • How many people they feel close to both online and offline • What type of social networking sites they use most often and how frequently • Quality of close relationships (Close Persons Questionnaire, CPQ) • Perceived social support (Multidimensional Perceived Social Support Scale, MPSSS)
(6) Well-being module (N=40)	• Self-assessment of personal characteristics (Wave 1 only, short form of the Big Five Inventory, BFI) • Anxiety and depression (Hospital Anxiety and Depression Scale, HADS) • Fatigue (PedsQL scale) • Physical Appearance (PedsQL scale) • Elements of the RAND 36-item Health Survey • Illness perceptions (Brief Illness Perceptions Questionnaire, bIPQ) • Spiritual Growth (Post Traumatic Growth Inventory-X, PTGI-X scale) • Subjective Well-being (Children's Worlds Survey) • Quality of life (Capability Wellbeing, ICECAP-A).

Table 3. Survey modules, number (N) and content of questions

7.3 Qualitative data

Qualitative data will be gathered via digitally-recorded semi-structured interviews pursued in the hospital when patients are attending clinics where possible, or over telephone/Microsoft Teams/Zoom or other organisation-approved and secure video-conferencing software as appropriate and approved within the Data management agreements in place within the University of Leeds and collaborating NHS sites. The role of interview will be to complement quantitative analyses with focus given to patient perceptions of disrupted biographies. Our Interview Topic Guide, which has been updated in consultation with our young study advisors can be viewed in Appendix 8. The interview will focus on the personal experiences, plans, and aspirations of patients at pre-diagnosis/during treatment/post-diagnosis related to (a) educational and work plans; (b) potential changes in their values and aspirations; (c) the

role of close friends and family before, during, and after treatment; (d) the most challenging or helpful factors in work, education and social relationships from diagnosis to post-treatment; and (e) the type of support they were offered and would have preferred during this time.

The structure and content of the interview may be further refined iteratively throughout the first 3 months of survey data collection to include any (a) emerging findings from Study 1 and 2; (b) preliminary emerging findings from the Survey; (c) advice from your Young Advisory Group (YAG) through our planned Patient and Public Involvement and Engagement (PPIE) activities (see below). Given the expected changes to the current version of the Interview Topic Guide, this will be the focus of a later amendment to this protocol.

7.4 Procedure

Surveys will be completed by consenting participants, while they attend NHS inpatient or outpatient visits, via post, or after being provided with link to an electronic version of the survey should they prefer an electronic assessment. Completion was estimated to take on average 30 minutes. Completion on site will utilise either a paper or tablet version. Remote paper completion is possible – participants will be offered a pre-paid envelope to return to the main research site in Leeds. If any participants should have difficulties filling in the Survey in written format, the team will be available to administer it verbally face-to-face or via telephone or video chat (Microsoft Teams/Zoom/other organization-approved audio-video-conferencing software). Interviews will be digitally recorded and conducted in private rooms on main site premises where possible or over the phone/video-chat where appropriate.

Participants will have 7 days to complete the survey once this is provided. Those who do not complete either wave of the survey will be sent two reminders at 2 and 4 weeks after the survey was due (Appendix 4); both reminders will include the link to the survey but only the second reminder will also include the survey in an electronic format (if communication takes place via email) or in hardcopy (if communication with the participant takes place via post).

A recruitment form (Appendix 10) in each recruitment site will monitor the recruitment progress, record the specific procedures utilised to administer the surveys (including Easy read or other accessibility requests) or run the interviews with each participant (e.g. mode of completion such as online, via paper, or verbally; location of completion – whether at home or remotely, etc.).

7.5 Study Timelines

Recruitment to the cohorts will begin in the first quarter of 2021, with the aim of recruiting, consenting and administering the Survey to 11-15 patients per month, per centre. All patients will receive a link to the electronic Survey or a paper version. Wave 2 of the Survey will be administered 6 months after they have completed Wave 1, allowing for +/- one month variation.

The interviews will be conducted between the two waves or following Wave 2, depending on the patient Cohort. Participants will be sent a PIS with a prompt image/instruction related to the interview between 1 and 2 weeks prior to the interview ‘windows’ as defined below. Namely, for Cohort 1 there will be some time-sensitivity to gather essential data at Wave 1 of the Survey. We will interview a sub-sample of this cohort (n = 25) people within a short ‘window’ following their diagnosis in order to capture the immediate impacts of cancer on

their SI. Consequently, 50% of this cohort will be interviewed within 3 weeks of first point of contact with the team (i.e. Wave 1). The remaining 50% will be interviewed within 6-8 weeks after receiving Survey Wave 2. Cohort 2 is less time-sensitive, since all respondents in this cohort are several years post-diagnosis. Here, however, there will again be two subsamples, but the driver will be our desire to capture and analyse some qualitative data from this cohort in order to revisit our Wave 2 questionnaire and ensure that it takes account of any emergent findings from the qualitative research, consistent with our mixed methods design. Therefore, 50% of the cohort will be interviewed within 6-8 weeks of the first point of contact with the team (i.e. Wave 1). The remaining 50% will be interviewed within 6-8 weeks of Survey Wave 2.

8 DATA ANALYSIS

8.1 Quantitative analyses

First, descriptive statistics and analyses of variance (ANOVAs) will be used to describe the SI outcome variables in our cohorts and how these vary by:

I. Time since cancer diagnosis/treatment (ten weeks post-diagnosis to 5 years post-treatment)
II. Explanatory variables identified in Studies 1 and 2, and relevant literature, including age group (16-24 and 25-39) and geographic location using linked ONS data on level of deprivation.

Second, appropriate regression models will be used to assess the role of time since diagnosis and the explanatory variables (identified above) in explaining differences in SI outcome variables using the data in our two cohorts. Appropriate goodness of fit measures will be used to assess the relative importance of different factors.

Third, data from the two cohorts will be pooled with the BRIGHTLIGHT and Understanding Society data that were used in Studies 1 and 2. Outcome and explanatory variables that are measured in at least one of the cohorts will be harmonised using a structured and systematic approach (Fortier et al, 2010).

The following analyses of the harmonised datasets will then be conducted:

I. Multivariable regression analyses will be used to enhance our understanding of the relationship between time since diagnosis/treatment and SI outcome variables that are measured in our own cohort study and BRIGHTLIGHT (the latter includes participants 6 months to 3 years after their cancer diagnosis which is not captured in our study: see Figure 2).
II. A case-control approach will be used to assess how SI outcome trajectories (for selected outcomes that are available across datasets) evolve over time for people who have had a cancer diagnosis compared to a matched control group of participants from the Understanding Society dataset who have never had a cancer diagnosis. Matching will be done using Propensity Score Matching using time-invariant characteristics and characteristics captured (retrospectively) in our own cohort prior to the cancer diagnosis (alternative matching methods will be conducted in sensitivity analyses). Multivariable regression analysis and latent growth modelling

methods (within the Structural Equation Modelling framework using e.g. the 'SEM' or 'LAVAAN' packages in R) will be used to compare SI outcome trajectories in the matched groups. These analyses will be conducted for the whole sample and stratified by the socio-demographic and clinical factors outlined as relevant in Studies 1 and 2, to better understand whether differences in SI trajectories (between people with and without cancer) vary between subgroups (e.g. by gender, ethnicity or cancer type).

Potential sources of bias will be assessed throughout the study. This will include (but not limited to) an assessment of:

I. The representativeness of the recruited participants when compared to the general population of TYA cancer survivors
II. The nature and pattern of missing outcome and explanatory variables within returned questionnaires. Dependent on the nature of missing data, appropriate methods of data imputation (e.g. multiple imputation by chained equations) may be considered for replacing missing values with plausible substitutes.
III. Sample attrition amongst recruited participants (i.e. loss to follow-up).
IV. Missing data due to the mortality associated with some cancer diagnoses, leading to survival bias (i.e. a logical error of concentrating on the people that made it past some selection process and overlooking those that did not, which can lead to false conclusions).

8.2 Qualitative analyses

Semi-structured interviews will be analysed thematically (Braun & Clarke, 2006). We will familiarise ourselves with the data, generate initial codes, search for themes, define them, and finally write a summary. These various stages will be iterative and will be undertaken by at least 2 members of the research group concomitantly (researcher triangulation). This will ensure the themes and subthemes arising are realistic and comprehensive. From the literature at the intersection of health inequalities, chronic conditions in young adults, and impact of cancer on life biographies in older patients, we know there is an impact of a cancer diagnosis on one's life journey. However, our qualitative approach will enable patients' own interpretations and experiences to emerge, pertaining to their own starting point, initial aspirations (shaped by their social context) and their trajectory after diagnosis.

8.3 Mixed methods data integration

We will integrate the quantitative and qualitative findings through an explanatory sequential design (Creswell, 2015), whereby quantitative secondary data will feed into any further amendments to the interview topic guide, followed by preliminary analyses of quantitative Study 3 data and initial interviews, which will further feed into any further interviews. Iteratively, initial findings/themes revealed in a subsample (approx. 10%) of interviews will also further feed into the quantitative data collection at Wave 2, if necessary. This means that the quantitative findings within the project will feed into the qualitative component and the latter will allow for the emergence of new themes or topics to be explored as part of the second wave, if appropriate.

Our updated Interview Topic Guide (Appendix 8) builds upon our review of relevant literature and previous surveys which inspired our own quantitative measurements.

In the end, we will draw the quantitative and qualitative findings to produce a model of the role of socio-demographic, clinical, psycho-social factors, and PROs over time, in predicting SI trajectories. This will ensure qualitative findings complement the interpretation of the quantitative results and allow for the emergence of any aspects of the TYAs' experience not previously accounted for in the literature.

9 ETHICAL CONSIDERATIONS

This study will be conducted in compliance with the Declaration of Helsinki, the General Data Protection Regulations (2018), Health Research Authority (HRA) approval and other regulatory requirements as appropriate.

Informed written consent will be obtained from the patients prior to any study-specific procedures. The right of a patient to refuse participation without giving reasons will be respected. The participant will remain free to withdraw at any time from the study without giving reasons and without prejudicing his/her further treatment/follow-up. The study will be submitted to and approved by the Sponsor, a main NHS/REC and the appropriate Site-Specific approvals prior to entering patients into the study.

Researchers involved in the study will have received GCP training honorary or substantive NHS contracts and adhere to NHS confidentiality guidelines and codes of conduct and will have access to a number of private spaces in the outpatients and ward areas in which to consent patients and carry out the study processes.

9.1 Confidentiality and anonymity

General policy: This study will be conducted in compliance with the Declaration of Helsinki, study protocol, the Data Protection Act (2018), General Data Protection Regulation (GDPR, 2018), the UK Policy Framework for Health and Social Care Research and will work in line with NHS and University of Leeds confidentiality policies and codes of conduct. The University of Leeds will act as study sponsor.

Hard copies of the Consent and Contact form (Appendices 3 and 12) will be stored at each research site. Namely, in Leeds these will be stored in locked filling cabinets in the restricted-access research offices of the University of Leeds, Section of Patient-Centred Outcomes Research, Level 6, Bexley Wing, St. James's University Hospital. In London these will be stored in a locked cupboard in the restricted-access offices of the UCLH Cancer Clinical Trials Unit. These forms will not be shared or transferred between the two collaborating centres.

Hard copies of forms which do not contain identifiable information, namely the survey and the CRFs, will be transferred, centralised, and stored in the University of Leeds office, separately from local Consent and Contact forms. Filling cabinet key access is restricted to the local study teams. Access to data stored on the University of Leeds secure server or NHS computers at both sites will be restricted to authorised local study staff only. Any participant surveys administered in hardcopy will be sent directly to the study staff in the University of Leeds by the participants in stamped, addressed envelopes. UCLH will send anonymised hardcopies of the CRFs to the study team in the University of Leeds via secure courier or scanned versions via secure NHS email (as applicable); in the University of Leeds

these will be stored and managed as detailed below. Participating sites will be required to keep electronic copies of this documentation on the secure NHS computers for auditing and quality control purposes.

Where temporary electronic storage of sensitive personal data is necessary (e.g. contact details for sending study documents/reminders/arranging wave 2 of the survey or the interview), files will be password protected, only accessible to relevant members of the local study team and stored on NHS computers in the respective study site (Leeds or London, depending on where a patient is recruited). Hardcopy consent forms and contact details will be kept at each study site and not be shared between University of Leeds and UCLH. The online consent to the survey will be stored in the University of Leeds online questionnaire software (QTool), for both Leeds and London participants who take the online survey. Consent for interviews (but not any other parts of the study) will include a statement related to the sharing of patient contact information between London and Leeds using a secure NHS email, to ensure sufficient manpower for conducting video/audio/text-recorded interviews across the two sites. This procedure will be implemented on a needs-basis except where an easy-read version has been recorded on the Recruitment monitoring form). In such instances the information will be communicated using NHS mail to study team members with an NHS Honorary or substantive contract.

While participants are actively participating in the study, their preferred contact details (postal address/email/telephone number), a preferred contact for a 'next-of-kin', their name and unique code will be stored on one password protected electronic file on a local, restricted-access NHS computer in each recruitment site. These files will not be shared across collaborating sites (apart from the situation defined above regarding interviews) and they will be destroyed for each participant, as they finalise their participation in the study. Hence, while the participants are actively in the study their data will be pseudo-anonymised. Once they finalise their participation in this study (defined as their last activity within the study, either wave 2 of the survey or interview), this information will be destroyed, the data becoming fully anonymised.

Each data collection form will display the unique participant code. The survey will collect partial data on patients' postcode (the first part and first digit of second part) and participants' month and year of birth. These will be used to calculate age and index of multiple deprivation. These two data points will be included in the electronic anonymised dataset which will be stored on University of Leeds computers for analysis purposes. Non-identifiable information which will be stored on University of Leeds computers for analysis purposes includes: clinical information, non-identifiable answers to surveys, redacted interviews. Redacted transcriptions will be stored on University of Leeds computers (and may be communicated to the study team in Leeds via NHS email by UCLH if needed).

Any manual files which can be transferred and need to be centralised in Leeds, namely surveys and CRFs will be, as applicable: a. sent by all participants directly to the Leeds study team in self-addressed, pre-paid envelopes (i.e. the Surveys); b. sent by the UCLH local study team to the University of Leeds study team in pre-paid envelopes (i.e. CRFs completed on site); c. stored in a secure, limited-access University of Leeds research office in St James's University Hospital, Bexley Wing, Level 6, in locked cabinets; d. stored in a

separate cabinet from any local physical consent forms and contact details; e. once received, the data will be transferred onto the University of Leeds electronic file, without partial postcode or month/year of birth (these will be transformed into the index of multiple deprivation and age while the information is transferred onto the electronic file).

Electronic data generated from the survey will be stored on QTool, the secure NHS-firewall protected questionnaire system, and exported as a spreadsheet on an NHS computer; paper-based surveys will be added to the same spreadsheet and a copy created without month of birth and partial postcode. This anonymised spreadsheet will be available for analyses and storage on the University of Leeds computing system.

Non-easy read consent forms for the interviews (but not any other parts of the study) will also include a statement related to the sharing of patient contact information between London and Leeds using a the secure NHS email, to ensure sufficient manpower for conducting video/audio/text-recorded interviews across the two sites. This procedure will be implemented only on a needs-basis, if a team member from Leeds or London had to cover the study team member on the other study site. Interview digital recordings will be transferred electronically, as soon as possible, from the recording device to secure password protected NHS/University of Leeds computers, only accessible by the research study team. Digital recordings and any transcriptions will be anonymised by the removal of identifiable information and use of a unique code. At this point, recordings and/or transcriptions can be stored and analysed on the University of Leeds computers. The original recording will be destroyed.
Interview transcription will take place in-house, with the support of a third party or via specialist software under appropriate GDPR and Data protection regulations. Interview transcription will be performed by hand in-house, with the support of a third party under a confidentiality agreement or if time is short, using an University of Leeds and NHS-approved transcription software which is GDPR compliant and the recorded interview will be deleted after transcription. The third party offering transcription support has extensive experience in collaborating with the University of Leeds and our research group (Typing Works) on the basis of a confidentiality agreement (available upon request).

If participants complete the consent form and survey electronically, no survey transfers will be necessary between Leeds and London, as data is automatically transferred onto the LTHT NHS server, but eligibility/withdrawal forms and any other anonymised CRFs will still need to be sent to the University of Leeds site via secure courier.

Upon identification, each patient will be assigned a unique study code. This study code will be used to pseudo-anonymise participant data and maintain confidentiality. The separation between identifiable data and anonymised data occurs at the point of eligibility screening with the allocation of a unique study code. A file linking the unique codes with the participants' name will be stored in an electronic format on the local NHS computer at each site. This document cannot be transferred between sites and will be destroyed at the end of the study. Any electronic transfers of data will be made non-identifiable.

Paper surveys with the original data will be stored on the University of Leeds premises in SJUH, Bexley Wing in locked file cabinets. Electronic surveys will be automatically transferred onto the NHS servers via QTool. They will be exported as an excel spreadsheet.

Information from the paper surveys will be added manually to the same spreadsheet. Once paper and electronic data are merged in the same spreadsheet on the NHS computer, the partial postcode and month/year of birth will be re-calculated into age and index of deprivation. The original spreadsheet will remain on the NHS computer. The de-identified spreadsheet will be moved onto University of Leeds computers for analyses.

Participants will be informed what will happen to their data through the PIS. Any publication or dissemination of the findings will be fully anonymised. Measures will be taken to ensure anonymity and confidentiality is not inadvertently breached through publication of small numbers. If numbers in analytic cells falls below 6, these will not be reported.

All researchers who have access to personal information are employed by the University of Leeds or Leeds Teaching Hospitals NHS Trust and have an NHS contract or an honorary NHS contract. The contract requires researchers to adhere strictly to NHS confidentiality guidelines and codes of conduct. All researchers have up-to-date GCP and Data protection training. Prior to starting work, all staff who have access to patient and research data undergo a DBS check. All researchers sign the Code of Conduct for non-clinical staff working with clinical data/samples for research purposes. The researchers have been granted permission by Leeds Teaching Hospitals NHS Trust to have limited access to the electronic patient record (PPM/PPM+) to view patient records solely for the purposes of research. All researchers are trained to use these systems before they are permitted limited access. Each researcher has an individual password to access PPM/PPM+, has 'read only access', and all activities are recorded and monitored. Researchers at UCLH are directly employed by the Trust in the Cancer Clinical Trials Unit and have up to date mandatory GCP training. They are trained to use the electronic health record system (Epic) and will access patient details and record study participation according to the Trust research policies.

Analyses will be conducted by the study team in the University of Leeds on anonymised data on the University of Leeds computers.

9.2 Protection from harm

It is possible that some of the questions used in this study may cover topics that for some may be uncomfortable. We will remind participants that they can skip questions which may make them uncomfortable and they can withdraw from the study at any time. Our teams in Leeds and London have conducted a number of large questionnaire and PRO research studies in the clinical setting (involving 2000+ patients) and our experience has shown that very few patients are distressed by the process of completing the measures or having interviews with researchers. In the PIS and Survey, participants are offered information on the main numbers they can call if they wish to discuss with someone about any areas they may have found concerning.

9.3 Assessment and management of risk

Our assessments of risk are as follows:

1. *The difficult process of recruiting patients to a cohort shortly after diagnosis and during follow up treatment leading to high attrition rates:*

The PI in Leeds as well as the Co-Investigators and project partners in both locations have extensive experience recruiting patients at post-diagnosis and throughout treatment. All study team members will be available to offer information and answer questions.

2. *Potentially uncomfortable topics involved in completing the questionnaires and interview*:

All questions included in the survey have been discussed with patient representatives to ensure they are not uncomfortable for any participants. The questions included are either based on validated instruments for this population or have been used extensively previously within the general population. Consequently, no questions or topics included should be troublesome.

However, patients are to be reminded throughout the process that they can withdraw from the study at any point without any influence on their treatment or care. Both the survey and interview schedules will be compiled through conversations with the YAG and will be purposefully structured to avoid being unduly emotive or burdensome. The interview Topic Guide and procedures have been amended in conversation with our YAG. Patients will be reminded that they can decline to complete parts of the survey and speak about any aspect of the interview which may feel uncomfortable.

3. *The potential that patients may die before being contacted for follow up*:

Before re-contacting the patients, the study team will check the patient's health status with the clinical team. Researchers will be granted consent by patients in order to review their status before re-contacting them. Patients will also consent to be contacted again and will provide their preferred method of contact which will be used to engage them during the study period. Any participant will be in the study for between 5-7 months, after which their contact details will be destroyed.

4. *Collection of minimally relevant contact and clinical data:*

As per Caldicott Guardian guidelines the purpose and use of any identifiable patient information will be clearly justified (i.e. name, date of birth/death, postcode, contact details). This information will be stored separately from any other information collected. Identifiable information will only be accessed and used by delegated members of the team for agreed purposes. For instance, contact details will only be stored (separately from any other information which will be anonymised) solely for patients to be re-contacted for the second wave of the survey and/or the interview. Once their participation in the study ends, their contact details will be destroyed (Contact details form, Appendix 12). Clinical information relevant to this study includes diagnosis, type of treatment, time since diagnosis and/or treatment, and the presence of other health conditions. Patients will be offering informed consent for this information to be accessed with the support of the clinical teams; this information will be collected using a bespoke CRF in an anonymised format. Storage of these types of information will be implemented under the principles of Good Clinical Practice.

9.4 Alternative arrangements: Accessibility

Arrangements are in place to ensure our study is fully inclusive (namely, all participants, from all walks of life, can participate in this study) and we are also compliant with Accessibility Regulations 2018. Consequently, the survey can be completed on any

computer with text-to-speech enabled or can be administered verbally, through a face-to-face, video-chat or telephonic conversation. While we ensured that all our supporting documents are appropriately accessible and terminology can be understood by a lay audience, a professional easy-read version is now also available. Braille and translated versions will be made available upon request.

9.5 COVID-19 contingency plan

COVID-19 (a highly contagious and potentially fatal strain of coronavirus) was declared a global pandemic on 11/03/20. The virus, which causes respiratory complications and flu like symptoms, poses a particular danger to our cohort. Immunocompromised patients have been advised to isolate at home and not make any unnecessary journeys, and all non-essential staff have been directed to work from home as of 23/03/20. Maintaining the safety of our participants is of the utmost importance, and as such we are creating a contingency plan to action should the situation continue as is currently, or in the event it becomes more serious. The main challenge is that face-to-face contact is reduced in cancer care services. It is likely that the TYA oncology wards and clinics in our target centres will restrict the presence of research staff. In such a case we propose the following alternate methods of data collection.

We will still attempt to identify and recruit participants using the methods above. Virtual clinics will or have been introduced as business as usual. That means we will still be recruiting participants through the local clinical teams for both Cohorts. In addition to this we will:

- Integrate our patient identification, approach, and monitoring procedures into the amended clinical processes of video calls, telephone clinics and letter-based patient monitoring that are in place.
- Any patient recruitment/eligibility/study-related discussion and questions will be held over the phone and/or online (Microsoft Teams/Zoom/other organisation approved audio/video-conferencing software)
- Information on the research can be given via post, email, over the telephone or by video call
- Participants will be required to fill out the consent form and send back an electronic/scanned copy while keeping a copy for themselves. The study team will make contact with their local clinical team, where possible, under informed consent
- Online survey administration will remain unchanged
- Interviews can still be conducted over telephone or a video conferencing platform.
- All information on data management and storage will remain unchanged.

This plan is merely precautionary; should the situation with the virus be under control and movement around hospitals authorised, we will follow the methods outlined previously in the protocol, subject to the policies and guidance issued by the University of Leeds and participating NHS trusts.

10 STUDY MANAGEMENT

10.1 Clinical Governance Issues

The overall clinical responsibility and welfare of the patients involved in the study will remain with the individual treating clinical teams within each disease group.

10.2 Local research management

Study management will primarily be undertaken within the regular (weekly/monthly/quarterly) internal meetings already held within the PCOR and London teams. Our study team comprising clinicians, nurses, the PI, CIs, researchers, patient representatives, other key external members of staff involved in the study at each of the sites will be responsible for the clinical set-up, on-going management, and promotion of the study. Updates to these individuals will be provided at least quarterly via our newsletter, email, teleconference or meetings in person if necessary.

The study team will be responsible for (i) protocol completion, (ii) case report form development, (iii) obtaining approval from the main REC and supporting applications for Site Specific Assessments, (iv) project initiation, (v) monitoring of screening, recruitment, data collection and follow-up procedures, (vi) auditing consent procedures, data collection, data validation, and database development and maintenance.

All participating sites will be expected to maintain a file of essential documentation (Site Specific File) and keep copies of all CRFs for the Study in the Investigator Site File. Hard copies of anonymised CRFs and survey will be stored and managed by the lead site. Each site is required to store and manage their own Consent and Contact forms ensuring they are stored securely, separately from any other patient information, and to keep an electronic version of anonymised study-related documents.

10.3 PATIENT AND PUBLIC INVOLVEMENT AND ENGAGEMENT (PPIE) - Youth Advisory Group (YAG)

Working within the guidelines set out by The Five Year Forward View (2014), NIHR guidance on PPIE and principles of 'what matters to you medicine', we intend to engage with members of the population we are studying throughout the project. In order to ensure this research is patient focused and patient led it is our intent to set up a Youth Advisory Group (YAG), consisting of a panel of TYAs who have experienced a diagnosis of cancer and treatment.

This group will be divided into two age groups 16-24 and 25-39, between Leeds and London, to keep in line with safeguarding guidelines and ensure that they are delivered in an age-and location-appropriate way. Recruitment to YAG will be done through advertisements, staff identified as a 'best placed-person', outpatient clinics and through local support groups. YAG information can be further disseminated through specific websites for TYA oncology support such as TCT, CLIC Sargent, Teens Unite, Ellen MacArthur Cancer Trust, Trekstock, Breast Cancer Now, CoppaFeel! and Shine. Members of the YAG will not be eligible for recruitment to the research cohorts.

The YAG will be comprised of a Core group, containing 6-8 young people (split evenly between the age and location) who will be actively involved in real time with the research, attending meetings, after having been trained on research methods and lay research communication.

They will offer active, creative, and critical insights into the progress of the project based on their lived cancer experience. This group will feed back any decision taken within the project meetings to a secondary group called the Wider TYA Network and their online/offline communities. The Wider YAG, containing 6-8 young people across ages and locations, will

attend at least one workshop/study team meeting per year, help promote the study on online platforms and offer remote feedback on any research-related public-facing materials.

Through the creation of the YAG we endeavour to create a dialogue between young people and clinical/research professionals. The YAG will play a key role in helping to brand and promote the study, refine the format of the questionnaire and the structure and content of the interviews. This will enable us to create person-focused work informed by patient's lived experiences of TYA cancer. Conversely, the YAG will also provide young people with opportunities to gain experience in research methods through our Core group. The Core group will be taught how to understand our research and contribute to our processes, with the aim that they attend steering meetings and support the communication between the study team and wider TYA communities. Their input will be of particular relevance for tailoring our communication with TYA cohorts in an age appropriate, accessible, and jargon-free manner. Throughout the intended lifespan of the project we aim to have a minimum of 4 engagement events. These engagement events will involve focus groups, workshops and presentations on the planned project and discussions around the content of our data gathering methods. In line with our COVID-19 contingency plan we will hold our YAG meetings virtually on a video conferencing platform in order to ensure the safety of its members.

In order to keep patients and the general public involved in the project over the course of its 3-year timespan, we will aim to have a website and biannual newsletters to track our progress. This will allow for patients involved in the study and the wider patient communities to keep up to date on how we are using their data and the future of the project. The YAG will also be involved in the dissemination of the results. Work will also be done using the YAG alongside youth theatres and arts groups to create an accessible and interactive summary of our findings. This will follow a similar route as the BRIGHLIGHT study which was formatted into a play involving young people called 'There is a Light', which was positively received and aided in further circulation of the research to a wider audience in a palatable format. Therefore, we aim to achieve similar results by disseminating our findings in real time via specific websites and social media channels.

11 DATA HANDLING AND MANAGEMENT

Data newly generated by our survey and interviews, unless otherwise specified, will be centralised and stored in the Study site files in the University of Leeds offices in the Leeds Cancer Centre, SJUH, Bexley Wing (as hard copies) and electronically within a shared secure drive on the secure University of Leeds server (on the N/P: drive) and NHS computers where access will be restricted to members of the local teams. Consent forms (Appendix 3) and Contact details (Appendix 12) will be kept as hardcopies on the recruitment sites in either of the 2 recruiting centres. Consent forms and contact details hard copy documents containing identifiable information will be stored separately from other anonymised study documents (eligibility form, withdrawal forms, survey etc) on the same premises of the UoL offices in SJUH, Bexley Wing. Both Leeds and London anonymised study documents will be stored in the UoL offices.

Electronic data generated from the survey will be stored on QTool, the secure NHS-firewall protected questionnaire system, and exported as a spreadsheet on an NHS computer; paper-based surveys will be added to the same spreadsheet and a copy created without

month of birth and partial postcode. This anonymised spreadsheet will be available for analyses and storage on the University of Leeds computing system.

New data generated through QTool will be pseudonymised through allocating patients a unique study code and link. A file linking the unique codes with the participants' name will be stored in an electronic format on the local NHS computer at each site. This document cannot be transferred between sites and will be destroyed at the end of the study.

Any potential data sharing between University of Leeds and UCLH will be anonymised and shared as encrypted files and then stored on an University of Leeds secure drive with access restricted to study team only. The only exception is the potential sharing of participant contact details via NHS mail between study team members in London and Leeds, for the purpose of ensuring sufficient manpower to conduct the interviews.

Consent forms for participants will be filed along with contact information, kept separate from questionnaires and CRFs to ensure anonymity. These forms will be kept on site both in Leeds and London and cannot be transferred. Paper copies of the data will be transferred onto the same electronic database on the NHS computer as the data generated by the electronic survey. They can be transferred as an electronic file onto University of Leeds computers (on the secure N/P: drives) after removal of month/year of birth and partial postcode. Interviews will be stored as digital files onto the secure N/P: drives at the UoL and then deleted from the recorder.

11.1 Data Monitoring

Routine data collection will be monitored for quality and completeness by the Data Manager, using verification, validation and checking processes. Missing data, will be chased until they are received or confirmed as not available (max 6 weeks after administering the Survey).

11.2 Archiving

Throughout the study original CRFs will be sent to and archived at the lead site (Leeds). Collaborating sites will all keep electronic copies of the CRFs and data collection instruments. At the end of the study, data will be securely archived in line with the sponsor's procedures, for 5 years (for non-CTIMP studies).

Newly generated data shared between UoL and UCLH will be anonymised and will not include patients name, date of birth or date of death. Files will be password protected before sharing through NHS emails.

Some of the data generated will be suitable for archiving and/or sharing provided that it is anonymised and does not contain sensitive clinical information. Secondary data from the general population surveys will be shared and stored in the Essex Data Archive. Some of the new data generated will be suitable for archiving and/or sharing if it is anonymised and does not contain sensitive clinical information.

Audio-files obtained in the qualitative component will not be available for sharing as their content may contain personal identifiable information. Qualitative data will be collected through anonymised audio-recorded interviews which will be deleted once transcribed with a redaction of any potentially identifiable information. Anonymised interviews transcripts will be shared and included in ESRC databases in the School of Sociology and Social Politics in the University of Leeds.

12 PEER AND REGULATORY REVIEW

This study has been peer reviewed by the University of Leeds ESRC Internal Panel, the National Cancer Research Institute National Research Group (21st February 2018) and by peer expert panels in the Economic and Social Research at point of funding.

These reviews included an in-depth evaluation of our conceptual framework, methodology, and quantitative and qualitative analyses.

The study has been peer reviewed in accordance with the requirements outlined by the University of Leeds, Leeds Teaching hospitals NHS trust and University College Hospitals London.

The study was deemed to require regulatory approval from the following bodies: NHS Research Ethics Committee, the Health Research Authority and R&D Departments at Leeds Teaching Hospitals NHS Foundation Trust and University College London Hospital NHS Foundation Trust. Each approval will be obtained before the study commences.

13 MONITORING AND AUDITING

The Principal Investigator will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

14 RECORDING AND REPORTING OF EVENTS AND INCIDENTS

Adverse effects are not expected to affect this research, in the manner they would be in other studies testing new cancer treatments. The study involves of a set of questionnaires and interview questions agreed upon by a panel of young cancer patients. However, we take adverse events very seriously and will use the following structure.

14.1 Definitions of Adverse Events

Term	Definition
Adverse Event (AE)	Any untoward medical occurrence in a patient or study participant, which does not necessarily have a causal relationship with the procedures involved in the research study.
Serious Adverse Event (SAE)	Any adverse event that: • results in death, • is life-threatening*, • requires hospitalisation or prolongation of existing hospitalisation**, • results in persistent or significant disability or incapacity, or • consists of a congenital anomaly or birth defect.
*A life- threatening event, this refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have	

caused death if it were more severe.

** Hospitalisation is defined as an in-patient admission, regardless of length of stay. Hospitalisation for pre-existing conditions, including elective procedures do not constitute an SAE.

14.2 Assessments of Adverse Events

Each adverse event will be assessed for severity, causality, seriousness and expectedness as described below.

Severity

Category	Definition
Mild	The adverse event does not interfere with the participant's daily routine and does not require further procedures; it only causes slight discomfort.
Moderate	The adverse event interferes with some aspects of the participant's routine, or requires further procedures, but is not damaging to health; it causes moderate discomfort.
Severe	The adverse event results in alteration, discomfort or disability which is clearly damaging to health.

Causality

The assessment of relationship of adverse events to the procedure is a clinical decision based on all available information at the time of the completion of the Clinical case report form.

The following categories will be used to define the causality of the adverse event:

Category	Definition
Definitely	There is clear evidence to suggest a causal relationship, and other possible contributing factors can be ruled out.
Probably	There is evidence to suggest a causal relationship, and the influence of other factors is unlikely.
Possibly	There is some evidence to suggest a causal relationship (e.g. the event occurred within a reasonable time after administration of the study procedure). However, the influence of other factors may have contributed to the event (e.g. the participant's clinical condition, other concomitant events).
Unlikely	There is little evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the study procedure). There is another reasonable explanation for the event

	(e.g. the participant's clinical condition).
Not related	There is no evidence of any causal relationship.
Not Assessable	Unable to assess on information available.

Expectedness

Category	Definition
Expected	An adverse event which is consistent with the information about the procedure listed in the Investigator Brochure, SPC, manual of Operation **or clearly defined in this protocol.**
Unexpected	An adverse event which is not consistent with the information about the procedure listed in the manual of operation **or clearly defined in this protocol.**

14.3 Recording adverse events

All adverse events will be reported to Principal Investigator at the respective study site. All Adverse events will be recorded following consent. All adverse events will be accompanied with a simple, brief description of the event, including dates as appropriate.

14.4 Procedures for recording and reporting Serious Adverse Events

All serious adverse events will be recorded in the medical records and the CRF. All SAEs must be recorded on a serious adverse event (SAE) form. The PI or designated individual will complete an SAE form and communicate this to the CI.

Completed forms for unexpected SAES must be sent within 1 working day of the Study team becoming aware of the event to the Sponsor, University of Leeds

Email forms to: governance-ethics@leeds.ac.uk

14.5 Reporting Urgent Safety Measures

If any urgent safety measures are taken the CI/ PI shall immediately give written notice to the relevant REC and Sponsor of the measures taken and the circumstances giving rise to those measures no later than 3 days from the date the measures are taken.

14.6 Protocol deviations and notification of protocol violations

A deviation is usually an unintended departure from the expected conduct of the study protocol, which do not need to be reported to the sponsor. The CI will monitor protocol deviations.

A protocol violation is a breach which is likely to effect to a significant degree:

(a) the safety or physical or mental integrity of the participants of the study; or

(b) the scientific value of the study.

The CI and sponsor will be notified immediately of any case where the above definition applies during the study conduct phase.

15 FUNDING AND SUPPLY OF EQUIPMENT

The study funding has been reviewed by the UoL and UCL/UCLH Research Offices and deemed sufficient to cover the requirements of the study. NHS costs will be supported via UCLH/LTHT and/or the Local Clinical Research Network. The research costs for the study have been supported by the Economic and Social Research Council (ESRC). Funding does not include any NHS support costs or additional researcher time. As a portfolio study, the study will be eligible for LCRN support, which will be negotiated on a Trust basis for administration support. All paper copies of questionnaires and stamped addressed envelopes will be supplied from the University of Leeds study office. An iPad with a protective case, encrypted to the University of Leeds standards will be provided under a loan agreement to the study team members in UCLH.

16 PUBLICATION AND DISSEMINATION POLICY

We propose 5 publications overall from the combined results of this study and studies 1 and 2. The objective of these publications will be to inform various academic groups on SI trajectories in TYAs. Results from this study will be presented to multiple professions specialising in TYA oncology care, developmental psychologists, psychosocial care providers, and in specialists in social medicine. In total we expect 5 publications to come from our findings. The planned integration of our mixed methods findings will be compiled into the proposed Multidimensional Stratification Model of Social Integration which we expect will be published in book format.

Dissemination of results will aim to impact upon the public through focused media activity. Work will also be done using the YAG alongside youth theatres and arts groups to create an accessible and interactive summary of our findings. This will follow a similar route as the BRIGHLIGHT study which was formatted into a play-based format titled ‘There is a light’. ‘There is a light’ was positively received and aided in further circulation of the research to a wider audience in a palatable format. Therefore, we will aspire to achieve similar results. We also aim to disseminate our findings in real time via specific websites and social media channels.

17 INTELLECTUAL PROPERTY

The intellectual property of the data generated will remain with the UoL. However, the University policy of the management of research data requires all data arising from research projects to be made openly available where possible. The research will not use any data which is covered by the Copyright, Designs and Patents Act 1988 or any other similar legislation.

18 INDEMNITY ARRANGEMENTS

The University of Leeds indemnity policy indemnifies the University against its legal liability to members of staff in connection with any injury suffered by them during the course of their

employment with the University. All accidents should be reported to the School or Faculty and the details entered onto Sentinel. In the case of serious injury, the Safety Services should be notified. Where necessary, statements should be taken from any witnesses immediately after the accident, photographs and first-aider statements are also useful for investigation purposes. This policy provides an indemnity to the University for its legal liability for injury to persons (other than employees) and damage to material property belonging to other persons arising in connection with the business of the University. The policy also provides an indemnity to staff and students acting on behalf of the University for their Legal Liability for accident or injury to other parties. The cover provided by this policy is in respect of claims which the University is legally liable to pay following breach of professional duty by reason of any neglect, error or omission on the part of an employee. The University of Leeds does not provide indemnity for non-negligent harm.

LTHT and UCLH will provide NHS indemnity cover for negligent harm, as appropriate and is not in the position to indemnify for non-negligent harm. NHS indemnity arrangements do not extend to non-negligent harm and NHS bodies cannot purchase commercial insurance for this purpose; it cannot give advance undertaking to pay compensation when there is no negligence attributable to their vicarious liability. NHS indemnity cover for negligent harm only applies to the employees of the two NHS Trusts (LTHT and UCLH), both substantive and honorary, conducting research studies that have been approved by the respective R&D Departments. The Trusts cannot accept liability for any activity that has not been Trust approved. Potential claims should be reported immediately to the Sponsor and the responsible R&D offices of the two NHS Trusts.

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