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Cohort profile: Do specialist cancer services for teenagers and young adults (TYA) add value? The BRIGHTLIGHT Cohort

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ABSTRACT

Purpose: International recognition of the unique needs of young people (YP) with cancer is growing. Many countries have developed specialist age-appropriate cancer services believing them to be of value. In England, 13 specialist Principal Treatment Centres (PTC) deliver cancer care to YP. Despite this expansion of specialist care, systematic investigation of associated outcomes and costs has to date, been lacking. The BRIGHTLIGHT Cohort was established to evaluate outcomes associated with access to PTCs for YP and associated costs to YP and the National Health Service (NHS).

Participants: Young people aged 13-24 years with a new tumour diagnosis between July 2012 and December 2014 were recruited from 97 NHS hospitals. A dataset has been generated of patient-reported outcomes at five time points over 3-years, clinical records and central NHS data from the BRIGHTLIGHT cohort.

Findings to date: A total of 1,114 participants were recruited: 55% (n=618) male, mean age was 20.1 years (SD=3.3), most (86%) were white and most common diagnoses were lymphoma (31%), germ cell tumour (19%) and leukaemia (13%). Thirty-four percent of YP had no involvement with the PTC, 40% had some and 26% received all care in a PTC over 12 months since diagnosis. At diagnosis, median quality of life score was significantly lower than a published control threshold (69.7 points); 40% had borderline-severe anxiety, and 21% had borderline-severe depression. There was minimal variation in other patient-reported outcomes according to age, diagnosis or severity of illness. Survival was significantly worse in the Cohort than for non-participants diagnosed during the same time period (cumulative survival probability 4 years after diagnosis: 88% vs. 92%).

Future plans: Data collection was completed in March 2018. Longitudinal comparisons will determine outcomes and costs associated with access/exposure to PTCs. Findings will inform international intervention and policy initiatives to improve outcomes for YP with cancer.

Strengths & limitations of this study

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5 bullet points

- This is the largest ever cohort of young people with cancer, examining not only cancer outcomes but also the social and educational impact of a cancer diagnosis.
- The socio-demographic characteristics of the cohort are broadly similar to the contemporary total teenage and young adult cancer population thus increasing the generalisability of results.
- Data has been collected from multiple sources, results therefore reflect the perspective of the patient, plus clinical care and data on health service use.
- Study results provide new information on cancer in young people and determines if access to a Principal Treatment Centre adds value; the relationships between specialist care and outcomes have previously been unclear. Findings will contribute to intervention and policy efforts to improve outcomes and patient experience for young people with cancer
- The cohort comprises 20% of young people diagnosed with cancer during the time period. A decrease from original target sample size (n=2,012) consequent of recruitment difficulties has resulted in a reduced statistical power to address the potential impact of heterogeneity within the cohort.

INTRODUCTION

BRIGHTLIGHT is a programme of research which aims to determine whether specialist care for teenagers and young adults (TYA) with cancer is associated with improved outcomes. The National Institute for Health and Care Excellence (NICE) outlined in the *Improving Outcomes Guidance for children and young people with cancer* [1] a model of specialised care based on a limited number of hospitals designated as principal treatment centres (PTC). At that time minimal information was available about either the constituent parts of such specialist care or the benefits that might accrue from it and why. BRIGHTLIGHT comprises six interlinked projects centred upon a prospective, longitudinal cohort of young people recruited soon after a diagnosis of cancer that examines their outcomes and experiences of cancer care. Additional studies address elements of specialisation; the environment of care [2, 3]; the competencies desirable in healthcare professionals delivering specialist care [4]; a metric to quantify specialist care; caregiver's experience of care; and a health economic analysis to determine the cost of specialist care. The programme has been underpinned by an extensive patient and public involvement strategy [5-9].

Cancer in young people is uncommon, accounting for less than 1% of all new cancer diagnoses in England [10]. Despite its rarity, cancer is the second leading cause of death for young people, accounting for 11% of deaths in those aged 15-24 years [11, 12]. In addition, a number of issues argue for special attention for young people with cancer and for robust evidence to support current and future healthcare policies. For example, young people present with a spectrum of cancer types that is distinct from those affecting younger children and older adults [11]. A cancer diagnosis during adolescence and young adulthood has an acute and unique impact on this critical and complex stage of life development, disrupting physical health, social and educational goals as well as psychological wellbeing [13]. These factors have additional importance when considered against the advantages which accrue to

society from the successful treatment through the prolonged fulfilment of their contribution in employment and other societal impacts [14].

While most young people are cured, outcomes for some cancers have not improved in line with those achieved for children and older adults [15]. There exists a general consensus among healthcare professionals that the needs of young people are poorly met by cancer services that are tailored towards the needs of children and older adults [16]. Young people fall between child and adult cancer services, into what has been described as either 'the grey zone' [17] or 'no man's land' [18]. Prolonged routes to diagnosis, unfavourable tumour biology with increasing age, limited access to clinical trials, lack of compliance with treatment protocols, inconsistent use of molecular diagnostics that may assist with optimal care, and a lack of specialist supportive care have all been implicated in the short fall in survival improvements[19-28].

Young people themselves have described unsatisfactory experiences of care which include: lack of recognition of their autonomy; failure to facilitate them to meet normal life goals during treatment; lack of peer support; care by staff with little experience of young people; and finally, inappropriate care environments [9, 29-31]. The inability of traditional healthcare silos to meet the unique psychosocial and healthcare needs of this specific population is increasingly highlighted [32-34]. Place of treatment and delivery of cancer care, in terms of both disease and age-appropriate specialist settings is increasingly acknowledged as potentially significant to the outcomes for young people with cancer [35, 36].

To address these unique needs and deficit in outcomes' knowledge, in August 2005 the NICE *Improving Outcomes Guidance* recommended that all care for patients under 19 must be provided in age-appropriate facilities and those aged 19 and over should have 'unhindered access to age-appropriate facilities and support when needed' [1]. To accommodate this recommendation thirteen TYA PTCs were identified across England. Key components of the services of the TYA PTC encompass tumour site-specific expertise delivered in conjunction with meeting the broader psychosocial needs of young people to support successful navigation of critical life transitions. This is directed through the TYA multi-disciplinary team (MDT) [1]. But, despite national guidance supporting this approach to the delivery of cancer care for young people aged 15-24 years [1] around half of young people continue to be treated in children's and adult cancer units with no or limited access to the TYA PTC, many receiving care in hospitals 'designated' by NHS commissioners to provide elements of specialist care that are available in a TYA PTC.

The aim of the BRIGHTLIGHT programme of research is to evaluate the benefit of specialist TYA cancer services for young people aged 13–24 years. The study has four key objectives specific to the cohort:

1. Relate the proportion of care young people received in a TYA PTC to: quality of life, satisfaction with care, clinical processes and clinical outcomes
2. Examine young people's experience of cancer care through a longitudinal descriptive survey
3. Compare social and educational milestones amongst young people receiving different levels of TYA cancer care
4. Determine the costs of specialist care to young people, their families and the NHS

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DESCRIPTION OF THE COHORT

Participants

The BRIGHTLIGHT cohort included young people aged 13-24 years, newly diagnosed with cancer (ICD-10 codes C00-C97) in an English hospital and recruited within four-months of diagnosis. Eligibility criteria were as inclusive as possible so no restriction according to language or a sensory impairment that affected communication was applied. The only exclusion criteria were: young people receiving a custodial sentence; if the young person was not anticipated to be alive at the first point of data collection (6-months after diagnosis); recurrence of a previous cancer or they were not capable of completing a survey, e.g. sedated and in intensive care.

Recruitment

Young people present with a wide range of cancer diagnoses [11]. It was anticipated that to identify and recruit potentially eligible patients would be the biggest challenge because of: 1) low incidence 2) presenting to numerous points in healthcare system, due to age and multiple diagnostic subtypes; and 3) inconsistent referral pathways for tertiary care. The NICE guidance was issued in 2005 [1], and by 2010 only 40% of newly diagnosed young people were known to a TYA MDT based at a PTC [37]. Analysis of the national cancer datasets between 2010 and 2011 indicated that young people were being treated in an additional 133 hospitals across England. Thus, to capture the full cohort of young people we needed to open recruitment in as many hospitals as possible, have a mechanism to identify young people across the country and also have access to an extensive network of researchers to recruit and administer the study questionnaires.

There were two mechanisms for identifying young people: first through the national Cancer Waiting Times (CWT) dataset, which has been reported in detail previously [38]. This is routinely collected NHS data used to monitor diagnostic and treatment targets; feasibility work suggested young people could be identified within three months of diagnosis [39]. However, when this method was applied nationally it was found to be neither timely nor accurate so a second mechanism was introduced: Principal Investigators were asked to liaise with the coordinators of all tumour-specific MDTs (except prostate cancer) so the person managing recruitment to the study could be informed of new diagnoses in young people aged 13-24 years. A third method to directly approach young people to invite them to participate was also introduced in the later stages of recruitment but did not significantly impact on accrual [40].

The second challenge was working with a very large number of hospitals, of which most were likely to identify a few eligible patients over the course of the study and who might present to one of several departments. BRIGHTLIGHT opened to recruitment in 109 hospitals, of whom 97 identified and recruited between 1-106 (median 5) young people per hospital, 12 not recruiting any participants. England has a national network of research personnel funded by the National Institute for Health Research (NIHR), tasked with facilitating recruitment into clinical studies [38]. The aim was to recruit 2,012 young people diagnosed between July 2012 and December 2013. Despite making multiple targeted amendments to the protocol and iteratively working with NIHR researchers and the TYA

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healthcare professional community to increase the proportion of patients who were offered study entry (supplemental file 1), recruitment was slower and lower than anticipated. In April 2014, an extension to recruitment until April 2015 was approved (young people diagnosed until December 2014, recruited within 4 months of diagnosis), and a lower target sample size was agreed (Figure 1).

Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures

i. Open to most Trusts agreeing to participate (n=77); posters to advertise BRIGHTLIGHT distributed to all Trusts
ii. Information to all newly diagnosed young people distributed in CLIC Sargent information packs; top recruiters reported in the TYAC weekly bulletin (the professional organisation in the UK supporting healthcare professionals with adolescents and young adults with cancer)
iii. Healthcare professional information leaflets sent to all Trusts (hard copy and electronic for local distribution)
iv. Director/Assistant Directors of the National Cancer Research Network emailed all the Cancer Network Managers directing them to make recruitment to BRIGHTLIGHT a priority; approved amendment to allow consent to be taken the same time a giving the information sheet
v. Review of screening logs and site specific feedback presentations sent to each Principal Treatment Centre (PTC)
vi. Open to recruitment in all 13 PTCs
vii. Approval to use social media to recruit young people; open in all 109 Trusts agreeing to open to recruitment
viii. Attendance at a Teenage Cancer Trust Lead Nurse event to highlight recruitment issues and gain support
ix. Emails sent by universities (communication teams or student unions) to current students with a link to the website to capture young people continuing with education after diagnosis; training for Youth Support Coordinators to be able to recruit young people
x. Attend a CLIC Sargent Social Worker event to promote the study and gain support to take a recruitment role
xi. Information on the BRIGHTLIGHT website in video format
xii. Recruitment method based on the National Cancer Patient Experience Survey implemented

Ethical approval and consent

The study was approved by London Bloomsbury NHS Research Ethics Committee (reference LO/11/1718). Approval by the Secretary of State under Regulation 5 of the Health Services (Control of Patient Information) Regulation 2002 was obtained from the Health Research Authority Confidentiality Advisory Group (reference ECC 8-05(d)/2011) to access the CWT dataset, Hospital Episode Statistic (HES) data and data from the National Cancer Registration and Analysis Service (NCRAS).

Data collection

Data were collected from three sources: young people, patient medical records, and central NHS and Public Health England (PHE) databases.

Data from young people

Patient-reported outcomes were collected from young people at five time points over three years: 4-7 months after diagnosis (wave 1), 12 months (wave 2), 18 months (wave 3), 2

years (wave 4) and a final data capture 3 years after diagnosis (wave 5). Data were collected using a study-specific questionnaire, the BRIGHTLIGHT Survey [41] (available under licence from https://xip.uclb.com/i/healthcare_tools/brightlight_wave1.html), which was administered as a face-to-face interview in young people's homes at wave 1. Subsequent waves were administered online or through telephone interviews. At wave 1, young people also completed study-specific health economics questionnaires, described below.

The BRIGHTLIGHT Survey

The BRIGHTLIGHT Survey is an investigator and young person-designed self-report questionnaire that was administered through computer-assisted personal, telephone or web interviewing or web by an independent research organisation. It was developed utilising patient-experience literature [42] and was underpinned by a conceptual framework to guide question content [9]. The BRIGHTLIGHT Survey contains five validated outcome measures and questions to reflect young people's experience of diagnosis and cancer care (Table 1) [41]. Completion of treatment occurs at different time points according to diagnosis. During the feasibility work young people emphasised that they did not want to be asked questions about cancer when treatment ended and therefore the computer administration of the BRIGHTLIGHT Survey had complex routing to ensure young people were only asked questions that were relevant to their current situation [41]. For example, questions related to pre-diagnosis and diagnostic experience were only asked at wave 1. The BRIGHTLIGHT survey also utilised 'pull through' options so that participants could reflect on responses given in previous waves before answering. For example, questions about employment/education goals were tailored so participants could be asked again at wave 5 to ascertain if goals had changed and if this was cancer-influenced.

Table 1: Summary of the content of the BRIGHTLIGHT Survey

Construct and questionnaire	Details
Quality of life – Pediatric Quality of Life Questionnaire (PedsQL™) [43]	Contains 23 items scored on a 5-point Likert scale. Four domains: physical, emotional, social and work/school functioning. Two summary scores (physical and psychosocial function) and a total score. Domain, summary and total scores on 0-100 scale, with 100 representing the best possible quality of life.
Health status – Euroqol- 5 Dimension 3 level (EQ-5D-3L) [44]	Comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) scored on 3 levels (no, some, severe problems). The EQ visual analogue scale records self-reported health on a vertical scale ranging from 'best imaginable health state' to worst imaginable health state'. Scores 0-1 with 0 representing death and 1 perfect health (negative scores represent a health state worse than death).
Anxiety and depression – Hospital Anxiety and Depression Scale (HADS) [45]	A measure of depression and anxiety. Contains 14 items, scored on a four-grade scale (0 to 3). Summary scores for depression and anxiety (ranging from 0 to 21). Scores of 8-10 are defined as borderline and 11 and over are considered moderate/severe anxiety and depression [46].

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Social support - Multi-dimensional Scale of Perceived Social Support (MSPSS) [47]	Scores for support by friends, family and significant others plus total support score. Contains 12 statements, rated on 7-point Likert scale. Total support score is an average ranging from 1-7, sub-support scores range 4 – 28. Total scale score 1-2.9 are considered low support; a score of 3-5 is considered moderate support; and scores from 5.1-7 are considered high support.
Illness perception - The Brief Illness Perception Scale (BIPS) [48]	Measures the emotional and cognitive representations of illness. Contains eight* questions with fixed response scale specific for each question, e.g. not at all – extremely helpful. Each question represents a different dimension of illness perception: consequence, personal control, treatment control, timeline, identity, coherence, emotional representation, concern. Responses scored 1 – 10, the higher the score the greater perceived illness impact. No overall score and each question represents a single domain.
Cancer experience questions [41]	Comprises of 12 experience domains: pre-diagnosis experience, diagnostic experience, place of care, contact with healthcare professionals, treatment experience, fertility, involvement in clinical trials, adherence, communication and coordination of care, education, employment, wellbeing and relationships. Total of 238 questions with question specific responses describing experience

*Timeline statement not included

Health economics questionnaires

Cancer/treatment related costs incurred by young people and families were collected using a study-specific Cost of Care Questionnaire and Cost Record. These included questions regarding: travel (car parking, petrol and capital depreciation, public transport); time off work; medical equipment use; prescription and over the counter drug use; cost of accommodation incurred through hospitalisation; complementary and alternative medicine; and cost of family care for siblings. The Cost of Care Questionnaire was administered at wave 1 and required young people and their families to record costs incurred from the above items retrospectively since diagnosis. The Cost Record was given at waves 1 and 2, requesting the same information collected prospectively, on a weekly basis.

Data from medical records

Research teams who recruited young people completed an electronic Case Report Form (CRF) 12 months after diagnosis, which contained key variables relating to diagnosis, treatment, clinical process and outcome variables. This included postcode at the time of diagnosis, locations of care, details of diagnosis, MDT treatment planning and care, and outcomes at 12 months after diagnosis. The Index of Multiple Deprivation (IMD) is a measure of socioeconomic status [49] and was derived from the postcode at diagnosis, based on the population denominator of England. Clinical processes of care were defined as *documentation of*:

1. Histological diagnosis
2. Molecular diagnosis
3. Cancer stage or prognostic group

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4. Initial treatment plan
5. Evidence of multidisciplinary communication
6. Assessment by supportive care services, defined as documented contact with a Clinical Nurse Specialist plus one other member of the MDT (social worker, youth support coordinator, counsellor, psychologist, dietician, physiotherapist, occupational therapist)
7. Fertility discussion
8. Consideration for inclusion in a clinical trial

Data from national datasets

Data from NCRAS and HES were used to supplement and validate details of treatment received in the TYA PTC, to support a detailed health economic evaluation based on hospital attendance and healthcare received, and to cross check against the e-CRF. NCRAS data included date of diagnosis, tumour morphology, staging and treatment data; and HES data included dates for admitted patient care (APC), outpatient and accident and emergency attendance, plus receipt of chemotherapy and radiotherapy.

Defining levels of care

BRIGHTLIGHT aims to evaluate exposure to specialist TYA cancer services, defined as treatment in the TYA PTC. In recognition that patients may receive elements of care in more than one hospital, we proposed that care could be categorised by three levels according to the proportion of care received in a TYA PTC. To accurately allocate cohort participants to the appropriate level of care, analysis of HES data were used. In summary, PTC Trust codes were identified for 2012-2014 and applied to HES data so the proportion of days spent in a TYA PTC in the first 6 months and 12 months after diagnosis could be calculated (details provided in supplemental file 2).

Defining severity of illness

Advanced cancer is associated with poorer quality of life [50, 51]. We planned to compare quality of life of those treated in different care environments. To do so, we needed to consider ways to control for differences between patients which might influence this outcome and in particular, the severity of their cancer. However, this is difficult for TYA as they present with a heterogeneous array of malignancies [11]. While most cancers have staging criteria which differentiate between more or less extensive disease (typically groups 1-4 in ascending order of worsening survival), stage is not directly comparable between cancer types and a comparison based purely on staging would be meaningless due to the variation in outcomes between different cancers allocated to the same stage level. For example, stage 4 thyroid cancer is associated with a much higher chance of survival than say, stage 4 bowel cancer. Furthermore, survival alone is a good indicator of severity of illness as it takes no account of disease and treatment morbidity both for the short and long term. We therefore developed a bespoke 'severity' grading system to include symptom and treatment burden as well as predicted survival and burden of late effects. Each cancer type was graded as least, intermediate and most severe based on cancer-specific information thus allowing comparisons between groups of patients with multiple types of cancer (Table 2; detailed methodology is presented in supplemental file 3).

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Table 2: BRIGHTLIGHT Severity of Illness Index (see supplemental file 3)

Cancer type [11]	**Least severe**	**Intermediate severity**	**Most severe**
Germ cell tumours	Stages 1-3; Stage unknown	Stage 4 (stage 1S=stage 4)	
Leukaemias	CML	ALL; Other and unspecified	AML
Non-Hodgkin lymphoma and non-specified lymphoma	Over 16yrs, protocol unknown Stage 1-2	Over 16s, protocol unknown; Stage 3-4; Any paediatric-type protocol; All unknown	Burkitts (ICD10 C83.7, morphology code 9687/3)
Hodgkin lymphoma	All stages		
Central nervous system tumours	Pituitary adenomas (D35.2); Sub-ependymal giant cell astrocytoma (C43.2)	Other completely resected WHO grade I tumours for which surgery is the only treatment needed - except craniopharyngiomas	Craniopharyngiomas; incompletely resected or unresectable grade I tumours; all grade II-IV tumours, any needing radiotherapy or chemotherapy. This includes ependymomas, medulloblastomas and intracranial GCTs
Bone tumours	Surgery only (low grade, periosteal, parosteal)		All other
Soft tissue sarcoma	Stages 1-2	Stage 3; Unknown	Stage 4
Rhabdomyosarcoma	Low risk EpSSG A-D[1]		All others; Unknown
Melanoma	Stages 1-2 (except 2c)	Stage 2c; Stage 3 (except 3c); Stage unknown	Stage 3c; Stage 4
Carcinoma	All thyroid; All Stage 1; Cervix stage unknown	Stages 2-3; All nasopharyngeal; Stage unknown (except cervix)	Stage 4
Miscellaneous and unspecified		All	

[1] EpSSG: European Paediatric Soft Tissue Sarcoma Study Group

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Characteristics of the BRIGHTLIGHT participants

A total of 1,126 young people were recruited for whom valid consent was available from 1,114 (Figure 2). Recruiting hospitals were required to keep a screening log, which was returned to the BRIGHTLIGHT team by 95 (87%) hospitals when recruitment ended. Of the 2,900 young people who had been screened, 429 (15%) were reported as not being eligible and 1,877 (65%) were eligible to participate. No details were provided for the remaining 594 (20%). Only 426 (23%) of those eligible had refused to participate, which was lower than the 35% we had anticipated and accounted for [8]. Of the 15% recorded as being ineligible, just over half (225, 52%) had either no reason recorded or appeared to have been deemed to be ineligible incorrectly.

Figure 2: A summary of participation at each wave of data collection

* Drop outs between waves due to death, permanent opt out or wave opt out. Wave-opt outs prior to being issued were not permanent opt-outs; participants could opt-out of a single wave but participate in subsequent waves; these cases were not removed from the cohort permanently

Data were obtained from NCRAS for young people diagnosed in the same time period, who were potentially eligible, i.e., alive 6-months after diagnosis and place of residence was not linked to a prison postcode. A total of 5,953 young people were diagnosed with cancer between July 2012 and December 2014, of whom 5,835 (98%) were potentially eligible to participate[1]; 1,114 (19%) appeared in the BRIGHTLIGHT Cohort.

FINDINGS TO DATE

Clinical and NHS data were available for all 1,114 young people. Of these, 830 (75%) completed the wave 1 survey (Figure 2). In total, 163 (20%) participated once, 186 (22%) twice, 195 (24%) completed three, 173 (21%) completed four and 113 (14%) took part in every wave.

Non-participants were similar in age and ethnicity to those in the BRIGHTLIGHT cohort but there were differences in gender (a lower proportion of males in non-participants) and inclusion by tumour type (a greater proportion of young people with leukaemia and lymphoma, germ cell tumours and bone tumours compared to non-participants but lower representation of brain tumours, skin cancers and carcinomas) (Table 3).

Table 3: Comparison of characteristics of participants and non-participants

		N	BRIGHTLIGHT Cohort	N	Non-Participants
Age at Diagnosis (years)	Mean (SD) Median (IQR)	1114	20.13 (3.28) 20.64 (17.58, 22.95)	4721	19.94 (3.33) 21 (17, 23)
Gender	Male Female	1114	618 (55%) 496 (45%)	4721	2213 (47%) 2508 (53%)
Ethnicity	White Asian Black	1085	936 (86%) 82 (8%) 22 (2%)	4316	3643 (84%) 288 (7%) 156 (4%)

[1] 109 young people died within 6-months of diagnosis so were assumed to be too sick to be approached and nine were in prison.

	Chinese		4 (<1%)		34 (<1%)
	Mixed		26 (2%)		74 (2%)
	Other		15 (1%)		121 (3%)
Type of cancer[1]	Leukaemia	1114	145 (13%)	4721	300 (6%)
	Lymphoma		350 (31%)		781 (17%)
	CNS		46 (4%)		735 (16%)
	Bone		102 (9%)		177 (4%)
	Sarcomas		78 (7%)		207 (4%)
	Germ cell		212 (19%)		504 (11%)
	Skin		45 (4%)		709 (15%)
	Carcinoma (not skin)		125 (11%)		1210 (26%)
	Miscellaneous specified		9 (<1%)		55 (1%)
	Unspecified malignant		2 (<1%)		43 (1%)
Geographical location[2]	Birmingham	1114	155 (14%)	4618	459 (10%)
	Bristol		116 (10%)		351 (8%)
	Cambridge		23 (2%)		276 (6%)
	Manchester		103 (9%)		391 (8%)
	Merseyside		42 (4%)		239 (5%)
	East Midlands		135 (12%)		278 (6%)
	Leeds		106 (10%)		254 (6%)
	Newcastle		59 (5%)		305 (7%)
	Oxford		19 (2%)		249 (5%)
	London (south)		77 (7%)		668 (14%)
	Sheffield		37 (3%)		174 (4%)
	Southampton		83 (8%)		221 (5%)
	London (north)		159 (14%)		753 (16%)

CNS: central nervous system; SD: standard deviation; IQR: interquartile range

[1] Based on the Birch classification [11]

[2] Hospitals mapped to the multidisciplinary team at the Teenage and Young Adult Principal Treatment Centre they were linked to

Of the 1,114 young people in the BRIGHTLIGHT cohort, 618 (55%) were male, mean age at diagnosis was 20.13 years (SD 3.28) and 936 (86%) identified themselves as white. Lymphoma was the most common cancer type (n=350; 31%), followed by germ cell tumours (n=212; 19%) and leukaemia (n=145; 13%) (Table 3). Table 4 details the sociodemographic and clinical characteristics of the BRIGHTLIGHT cohort. There was an even distribution across socioeconomic groups. Most were single (n=606; 84%) and employed or in education (n=531; 64%). Systemic anti-cancer therapy was the most common form of treatment, used for 880 (79%). Thirty (3%) young people received no treatment, just active monitoring. The clinical processes that were most frequently documented in the clinical records were MDT communication (n=1037; 97%), cancer stage or prognostic group (n=1015; 94%), histology (n=974; 91%) and initial treatment plan (n=974; 91%). One hundred and sixty seven (20%) young people reported having a pre-diagnosis long-term condition.

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Table 4: Socio demographic and clinical characteristics of the BRIGHTLIGHT Cohort

Characteristic		Number	%
Socioeconomic status (IMD quintile) (N=1088)	1 – most deprived	250	23
	2	194	18
	3	209	19
	4	230	21
	5 – least deprived	205	19
Marital Status (wave 1; N=725)	Married/civil partnership	26	4
	Cohabiting	93	13
	Single/divorced	606	84
Current status (at wave 1; N=830)	Working full/part time	257	31
	In education	274	33
	Other work (apprentice/intern/voluntary)	17	2
	Unemployed	31	4
	Long term sick	126	15
	Not seeking work	125	15
Length of inpatient stay over 12 months (N=1070) days	Median (IQR)	25	9 to 74
Treatment (N=1114)[2]	Systemic anti-cancer therapy	880	79
	Radiotherapy	324	29
	Surgery	551	50
	Active monitoring	30	3
	Transplant (stem cell or bone marrow)	28	3
Severity of illness (N=1114)	Least	611	55
	Intermediate	254	23
	Most	249	22
Clinical processes of Care (documentation available in clinical records)	Histological diagnosis (n=1072)	974	91
	Molecular diagnosis (n=737)[3]	258	35
	Cancer stage or prognostic group (n=1078)	1015	94
	Initial treatment plan (n=1071)	974	91
	MDT communication (n=1074)	1037	97
	Assessment by supportive care services (n=1057)	563	53
	Fertility being discussed (n=1063)	693	65
	Consideration into a clinical trial (n=1057)	676	64

CNS: central nervous system; IMD: Index of Multiple deprivation; IQR: interquartile range

[1]Based on period of 12 months from diagnosis. Missing for 70 participants: 26 had no days in hospital after diagnosis (inpatient stay was before diagnosis date) and data were missing for 44

[2] N greater than 1114 reflects multiple treatment modalities for some diagnoses

[3] Where relevant, indicated as not relevant in 320

A total of 124 (11%) young people in the BRIGHTLIGHT cohort died before 31st December 2016. Results from cox regression indicate that the survival benefit for non-BRIGHTLIGHT patients was maintained even after adjustment for age, gender, ethnicity and type of cancer; the risk of death was 34% higher for those in the BRIGHTLIGHT cohort compared with those not in the cohort. (Figure 3; hazard ratio estimate 1.34 (95% confidence intervals 1.09-1.68), p=0.01). The reason for this difference is unclear.

Figure 3: Comparison of survival between participants in the Cohort and non-participants[1]

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Estimated cumulative survival probabilities by year from diagnosis (95% CI)		
	Non BRIGHTLIGHT	BRIGHTLIGHT cohort
1 year	0.98 (0.97, 0.98)	0.98 (0.97, 0.99)
2 years	0.95 (0.94, 0.96)	0.92 (0.91, 0.94)
3 years	0.93 (0.92, 0.94)	0.89 (0.87, 0.91)
4 years	0.92 (0.91, 0.93)	0.88 (0.85, 0.90)

CI: confidence intervals
Log rank test P value <0.0001
[1]Non-participants were young people diagnosed in the same time frame as the BRIGHTLIGHT cohort identified by the National Cancer Registration and Analysis Service (NCRAS), who were not part of BRIGHTLIGHT

A summary of patient-reported outcomes recorded at wave 1 are presented in Table 5. Mean total quality of life, physical and emotional domains scores were <69.7 indicating young people were at high risk of impaired quality of life shortly after diagnosis [52]. Forty percent of young people could be classified as 'cases' for anxiety and 22% for depression (borderline-severe) [46]. Young people reported high levels of support from friends (Multi-dimensional Scale of Perceived Social Support cut off >5) and moderate support from family and significant others (score 3-5) [47]. The Brief Illness Perception Scale results indicate that young people felt cancer had a moderate effect on their life but they perceived that treatment was extremely helpful. They perceived themselves as having experienced a moderate number of symptoms and believed they had a good understanding of their cancer. The majority rated their satisfaction with care as being excellent/good (n=777; 94%). Those aged 19-24 years seemed to have better physical and psychosocial quality of life compared to those aged 13-18 years at diagnosis. This older age group also reported more anxiety, lower social support, better perceived personal control but lower perceived emotional representation and concerns. According to diagnosis, young people with a solid tumour had better physical scores, perceptions of consequences and identity but less support from friends than those with a blood cancer. Finally, there was a noticeable trend for better total quality of life, physical and psychosocial scores for those with less severe disease and worse emotional score for the intermediate severity group. Young people with less severe disease had better perceived consequences and identify but satisfaction with care was highest in those with the most severe disease.

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Table 5: Summary of the wave 1 patient-reported outcomes

			Age		Diagnosis		Severity of illness		
Characteristic	**N**	**All patients N=830**	**13-18yrs N=302**	**19-24yrs N=528**	**Haematology N=373**	**Oncology N=457**	**Least N=461**	**Intermediate N=194**	**Most N=175**
PedsQL - mean (SD)									
Total score	829	66.20 (19.79)	64.14 (18.53)	67.39 (20.40)	64.59 (18.28)	67.52 (20.86)	70.67 (18.86)	61.55 (19.77)	59.57 (19.25)
Physical summary score	828	59.45 (27.72)	54.67 (26.75)	62.20 (27.91)	56.96 (25.04)	61.47 (29.58)	67.65 (25.49)	52.67 (26.63)	45.33 (26.95)
Psychosocial summary score		80.38 (18.45)	77.88 (18.27)	81.82 (18.42)	79.37 (18.49)	81.21 (18.41)	84.15 (16.75)	75.90 (19.82)	75.43 (18.98)
Emotional summary score		67.64 (22.76)	70.94 (21.83)	65.75 (23.07)	67.75 (21.68)	67.55 (23.62)	68.05 (23.09)	64.92 (23.15)	69.57 (21.21)
EQ-5D – mean (SD)	830	0.76 (0.24)	0.75 (0.23)	0.77 (0.24)	0.77 (0.22)	0.76 (0.25)	0.81 (0.21)	0.71 (0.26)	0.71 (0.24)
Total score									
- **median (IQR)**		0.80 (0.69-1)	0.80 (0.62-1)	0.81 (0.69-1)	0.80 (0.69-1)	0.80 (0.66-1)	0.85 (0.73-1)	0.73 (0.62-1)	0.75 (0.59-0.88)
HADS – mean (SD)[1]	830								
Anxiety score		6.89 (4.39)	6.14 (4.12)	7.32 (4.49)	6.79 (4.36)	6.98 (4.43)	7.23 (4.55)	7.01 (4.44)	6.14 (3.83)
- Borderline n (%)		160 (19%)	51 (17%)	109 (21%)	75 (20%)	85 (19%)	82 (18%)	44 (23%)	34 (19%)
- Moderate/severe n (%)		172 (21%)	48 (16%)	124 (23%)	70 (19%)	102 (22%)	106 (23%)	40 (21%)	26 (15%)
Depression score		4.62 (3.68)	4.45 (3.38)	4.71 (3.84)	4.84 (3.57)	4.43 (3.76)	4.31 (3.65)	5.16 (3.79)	4.81 (3.57)
- Borderline n (%)		120 (15%)	40 (13%)	80 (15%)	48 (13%)	72 (16%)	48 (10%)	40 (21%)	32 (18%)
- Moderate/severe n (%)		55 (7%)	16 (5%)	39 (7%)	26 (7%)	29 (6%)	32 (7%)	14 (7%)	9 (5%)
MSPSS – median (IQR)									
Total support	820	1.50 (1.08-2.25)	1.58 (1.17-2.33)	1.50 (1-2.08)	1.58 (1.08-2.25)	1.42 (1.08-2.17)	1.50 (1.08-2.25)	1.58 (1-2.25)	1.50 (1.17-2.08)
Support - friends	827	7 (4-11)	7 (4-12)	6 (4-10)	7 (4-11)	6 (4-10)	7 (4-10)	7 (4-12)	7 (4-10)
Support - family	827	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	4 (4-7)
Support – significant others	823	4 (4-8)	5 (4-9)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-9)	4 (4-7)
BIPS – median (IQR)	830								
Consequences		7 (4-8)	7 (5-8)	7 (4-8)	7 (5-8)	6 (4-8)	6 (4-8)	7 (5-8)	7 (6-9)
Personal control		6 (4-8)	6 (5-8)	5 (3-8)	6 (4-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Treatment control		10 (9-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (9-10)	10 (8-10)
Identity		5 (3-7)	6 (3-8)	5 (3-7)	6 (4-7)	5 (2-7)	5 (3-7)	6 (3-8)	6 (4-8)
Coherence		8 (7-10)	9 (7-0)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	9 (7-10)
Emotional representation		6 (4-8)	5 (3-7)	7 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (3-8)
Concern		6 (3-8)	5 (3-7)	7 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Satisfaction with care – n (%)	820								
Excellent/good		777 (95%)	284 (95%)	493 (95%)	358 (96%)	419 (94%)	433 (95%)	173 (91%)	171 (99%)

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Fair/poor/very poor		43 (5%)	16 (5%)	27 (5%)	15 (4%)	28 (6%)	23 (5%)	18 (9%)	2 (1%)

BIPS: Brief Illness Perception Scale; EQ-5D: Euroqol 5-Dimension; HADS: Hospital Anxiety and Depression Scale; IRQ: interquartile range; MSPSS: Multi-dimensional Scale of Perceived Social Support; PedsQL: Pediatric Quality of Life Questionnaire;SD: standard deviation

[1]Borderline = 8-10, moderate/severe = >11 [46]

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STRENGTHS AND LIMITATIONS

The BRIGHTLIGHT cohort is the first national, prospectively recruited cohort of teenagers and young adults with cancer. We are able to examine in detail the complexity associated with place of care, experience and outcome. This is made possible through the use of linked data from multiple sources so unlike other cohorts which rely solely on patient-reported outcomes [34, 51] or clinical data [32], a more comprehensive evaluation can be derived. Using national mandatory NHS datasets we have been able to calculate a more robust measure of time spent in specialist TYA care. Other data sources, such as secondary analysis of the National Cancer Patient Experience data is based on TYA PTC code at the time of participation [53], as such this reflects a single point in time and does not reflect experiences and outcomes for those who have exposure to both specialist and non-specialist care. Measuring exposure to a TYA PTC through analysis of HES data has enabled a more objective exposure variable to be developed. Similarly, defining severity of cancer through prognosis for survival alone does not reflect the symptom/treatment burden of disease and the impact this has on quality of life during treatment and recovery. Systematically defining prognosis alongside symptom and treatment burden, provides a more nuanced measure and is a better reflection of the severity of illness.

Selecting the study design to evaluate TYA cancer services across England was challenging as services were already in place and, in some regions of the country, long-established. There was also wide variation in implementing the NICE Guidance [1] according to local need and pre-existing resources, resulting in services at PTCs not being identical. The decision to establish a cohort was made on the basis that it is suited for investigating rare exposures, allows examination of multiple outcomes for the defined exposure (to specialist care), and would enable us to gather data regarding sequence of events, with the potential to assess causality. The main limitation of the cohort is we only recruited a fifth of the population who were eligible to participate. Variation in diagnosis and severity between those in the cohort receiving different level of PTC care reduces the potential to assess causality.

Cohort studies are acknowledged to be challenging to establish and maintain, especially in rare conditions due to the requirement for large numbers of subjects, potential for selection bias and the challenges associated with subject retention [54-57]. We anticipated that participation might favour those who were less unwell or had a better prognosis. The inclusion of significant numbers with tumours associated with poorer prognosis such as bone tumours and the inferior survival of the cohort go against this. Our experience of recruitment points to the value of maintaining accurate screening logs and seeking mechanisms to complement the intelligence from local teams about change of status of participants such as death or change of address.

Our experience highlights the value of patient and public participation in research. The focus of this study was identified by young people as a priority area for research. Young people joined the research team to work as co-researchers to develop the grant application [6, 9]. They are co-applicants on the grant and have been integral in naming the study [5], study management [7, 8] and dissemination. In total more than 1,200 young people have been involved in BRIGHTLIGHT as part of the research process almost the same number as

those recruited. We believe this has positively influenced the rates of participation, ways in which young people were approached and methods of data collection, and doubled the retention rate at Wave 3 [7].

This population is known to have lower involvement in clinical trials in comparison to children and older adults [22, 58], yet there have been no targeted interventions developed to improve recruitment [59]. We have reported that to optimise recruitment to clinical trials, what we have identified as 'the 5'A's' need to be addressed, namely availability, accessibility, awareness, appropriateness, and acceptability [58]. We have identified factors that young people feel are acceptable for accessing research [8] and for continuing their involvement in a study [7]. We have also identified that the networked structures for facilitating recruitment into cancer research in England may not be optimal for the recruitment of young people [38]. The impact of not having an optimal research network was made apparent through BRIGHTLIGHT, as it was the first national study in this population. Ways to overcome this challenge are currently being explored by the NIHR.

FUTURE PLANS

The BRIGHTLIGHT cohort was originally designed to evaluate short-term outcomes, from early after diagnosis to three years after diagnosis, over five time points. Data collection for wave 5 ended in February 2018, with results for the four key objectives anticipated to be available by the end of 2018. As noted earlier, the study has generated a large quantity of data and with the recent completion of a James Lind Alliance Priority Setting Partnership exercise for TYA exercise (http://www.ncri.org.uk/ncri-blog/top-10-research-priorities-for-teenage-and-young-adult-cancer-identified/), there is the opportunity to address some of the unanswered questions with the BRIGHTLIGHT cohort. This opportunity has already been realised to contribute evidence to improvements in early diagnosis [19]. In line with NIHR guidance, patient-reported outcome data from the cohort will be made available to external researchers on acceptance of the final report in the NIHR Journal Library. Details of how to apply will be made available on the website (www.brightlightstudy.com).

The philosophy of specialist TYA cancer care is to provide optimal cancer treatment alongside the developmentally-sensitive care that enables young people to achieve their life goals (e.g. education, employment, relationships) during treatment and beyond. BRIGHTLIGHT will evaluate this in the short-term but longer-term follow-up may be valuable to explore whether the model of care delivery influences these outcomes later in life. We are now planning a 10-year follow-up study to assess the long-term impacts. We also acknowledge that similar to other studies quantifying care using NHS data [53, 60], the measure of specialist care may lack discrimination, not least because it assumes that all TYA PTCs and other places of care are equal. Additional to the cohort, a case study was conducted to understand the culture of TYA cancer care [3]. There is the potential to synthesise the qualitative findings from the case study with the quantitative data from the cohort to develop a more detailed and sensitive metric to define specialist TYA cancer care. Ultimately, the data generated by the cohort and BRIGHTLIGHT will provide new information on cancer in young people and determine if access to a PTC adds value. The relationships between specialist care and outcomes have previously been unclear. Findings will inform intervention and policy efforts to improve outcomes for young people with cancer.

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RMT, LAF, JB, DS, SM, RF, LH, FG, RR, JSW were involved in developing the protocol. RMT coordinated the running of the study and was responsible for data acquisition. JB, JGA, RMT, LAF, SM, RF, DS, JSW contributed to the analysis. RMT, LAF, JB and JSW drafted the manuscript. All authors critically revised and approved the final manuscript.

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The Quality of Life study described in this paper was carried out using the PedsQL, developed by Dr. James W. Varni.

Competing interests:
None declared.

Ethics Approval:
The study was approved by the Health Research Authority Confidentiality Advisory Group (reference ECC 8-05(d)/2011) and London Bloomsbury NHS Research Ethics Committee (reference LO/11/1718).

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Data sharing statement:
Further details of the BRIGHTLIGHT programme of work is available through the study website (www.brightlightstudy.com). Data that are not held under licence with Public Health England or NHS Digital will be available from late 2018 when the primary analysis is complete. We welcome collaboration, for general data sharing enquiries please contact RMT (rtaylor13@nhs.net).

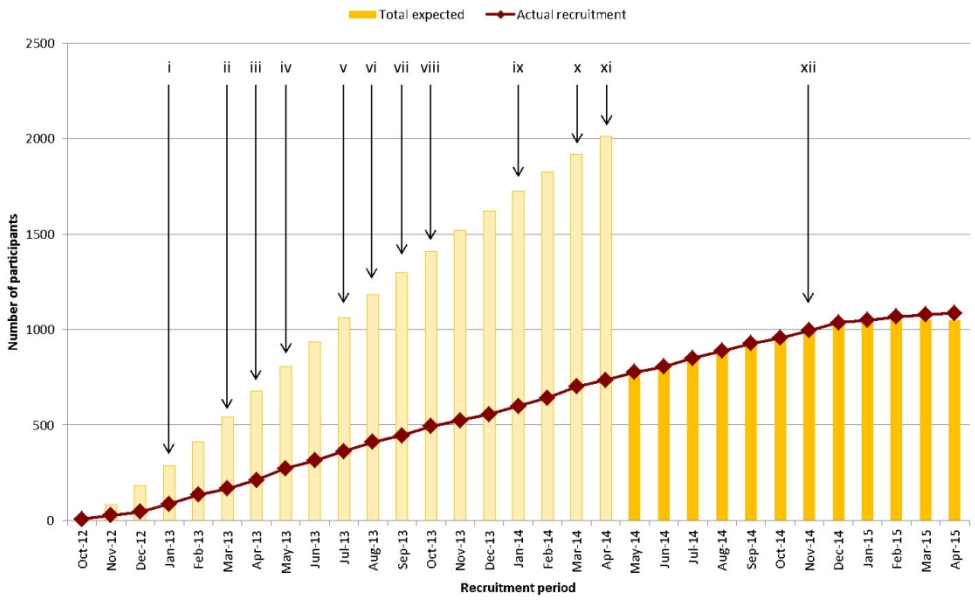


Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures

514x319mm (72 x 72 DPI)

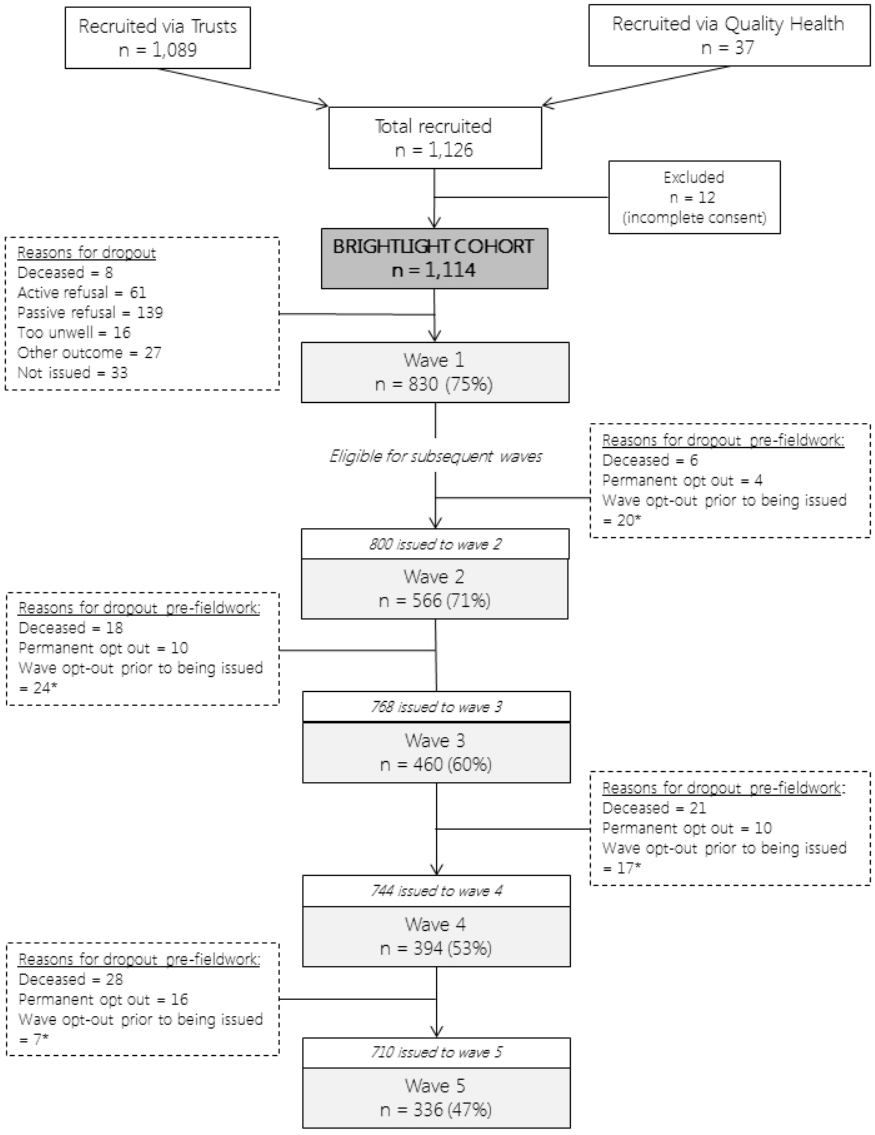


Figure 2: A summary of participation at each wave of data collection

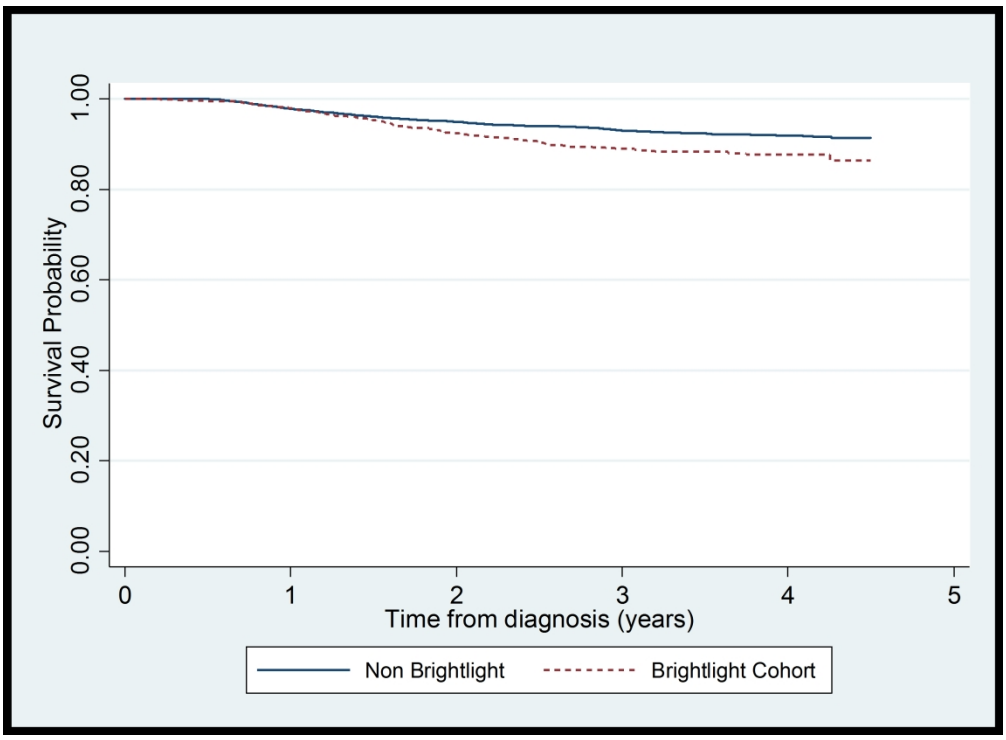


Figure 3: Comparison of survival between participants in the Cohort and non-participants

BRIGHTLIGHT Cohort profile – supplementary file 1

Supplementary File 1 Detailed results of actions implemented to improve recruitment to the cohort

Table A: Possible challenges reported by healthcare professionals before recruitment began and strategies identified to overcome them

	Challenges	**Strategies proposed to overcome challenges**
Identifying young people	Missing eligible young people if transferred to regional specialist centres Recruiting across a range of hospital sites Recruiting across multiple tumour types Engaging consultants: one concern was they would not think the older TYAs were eligible, a perception being that it was a 'teenager' study	Use the TYA MDT meetings to identify young people Co-ordination by a key person such as the Lead Nurse, cancer network head, or MDT lead to ensure details of eligible TYAs are passed to the recruiters Collaborative working with other centres to ensure all young people are approached, but not on multiple times
Approaching/consenting young people	Concerns about 'getting past' protective and upset parents Timing of consent, particularly if the patient is undergoing chemotherapy and was likely to be feeling very unwell Lack of experience in working with 'children' Being seen or felt to 'pressurise' potentially 'vulnerable and fragile' young people to take part Getting treating consultant approval to approach young people	Encouraging the initial approach to be a conversation, and not be immediately about persuading young people to take part Work with paediatric nurses to help with recruiting younger TYA Undertake paediatric consent training Wait for a sufficient length of time after diagnosis – maybe two months – before introducing the study, to allow the young person to become accustomed to the emotional and practical impact of the diagnosis

TYA: Teenage and young adult; MDT: multi-disciplinary team

BRIGHTLIGHT Cohort profile – supplementary file 1

Table B: Suggestions from healthcare professionals for keeping young people engaged throughout the study

Suggestion to keep young people engaged	**Action for implementation by BRIGHTLIGHT**
Get the consent process absolutely right: clear, accurate information about the survey, as buy-in from young people will increase the chances they will continue to participate	Information developed with young people, site initiation with recruiters to ensure they knew about the study and could relay information to young people in the best way
Provide TYA-friendly formats: e.g., ensure the survey could be completed on an iPad or iPhone as well as on a home computer	The survey was administered face-to-face at the first time point; subsequently it could be completed online on any platform
Use the internet: communicate via social networks like Facebook and Twitter	An open Facebook account was prohibited by the sponsor Trust but a Twitter account was opened
Ensure language used is aimed at empowering young people	All information was reviewed by the YAP[1] and had a reading ease of >70%
Consider incentives: e.g., a medal-based reward system – for each year young people remain in the study they move up the medals from Bronze (Year 1) to Silver (Year 2) and Gold (Year 3) and get a correspondingly increasingly valuable reward each time.	The YAP suggested a reward system using wrist bands with a different colour for each wave of participation
Inform participating young people on why the study matters and why their continuing involvement is important	A website was developed to keep young people updated about the programme www.brightlightstudy.com
Maintain contact throughout	Newsletters
Disseminate progress and results so they can see the wider scale and impact of the survey, that is making a difference	Content of newsletters related to results as far as was possible
Keep parents on board perhaps with targeted communications	Newsletters sent to all the email addresses provided
Distribute posters and flyers to treatment centres	Posters and flyers provided

YAP: Young Advisory Panel; TYA: teenage and young adult

[1]YAP are the BRIGHTLIGHT patient user group

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C: Suggestions for how the BRIGHTLIGHT Team might facilitate recruitment and actions taken to address these

Suggested change	Action by the BRIGHTLIGHT Team
1. Study information for health professionals	An information booklet was developed giving a brief summary of the study. This was sent electronically and as hard copies to all participating Trusts. Regular newsletters were developed and circulated online and as hard copies. Recruitment figures were circulated in a weekly Bulletin by TYAC to their members and were also Tweeted by the BRIGHTLIGHT team (@bR1GhTLiGhT)
2. Make the participant information sheets as short as possible	A summary booklet had been produced by Ipsos MORI[1] to send as a reminder about the study by their interviewers. An ethics amendment was made in July 2013 to allow this to be used in conjunction with the lengthy information sheet at the time of consent. Video versions of the information sheet were made available on the website (www.http://www.brightlightstudy.com/user-involvement/)
3. Investigate any variation in recruitment rates between sites	Screening logs were requested and analysed to identify reasons for suboptimal recruitment, which was fed back to each Trust with guidance on how to overcome recruitment issues.
4. Reduced interval between giving information and getting consent[2]	An amendment was approved by the Ethics Committee to allow consent to be taken within the same 24-hour period as information was given.
5. Provide BRIGHTLIGHT advertising materials	Posters, flyers and postcards had been available since the beginning of the study. These were distributed not only by the BRIGHTLIGHT Team but also by CLIC Sargent and Teenage Cancer Trust.
6. Keep sending the NWCIS notification[3]	There was a temporary pause in the CWT data being sent due to organisational change of NWCIS to Public Health England.
7. Extend the window of recruitment for wave 1	This was relaxed at the end of 2012 so young people could be recruited at any time in the first four months after diagnosis. We were unable to extend recruitment beyond this period because we wanted data to be collected within a specific time window. Young people were not able to enter the study at later time points because subsequent questions were informed by responses in the first survey.

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C. *cont.*

Suggested change	Action by the BRIGHTLIGHT Team
8. Reduce the number of times young people need to participate (total study participation involved 5 time points in 3 years)	The sample size calculation was based on participation at three time points (as specified in the protocol) because we were aware young people might opt in and out of participation depending on their current life commitments. We developed top tips for recruiting Trusts, including information about participation. The top tips were prominent on the website, were sent as an information leaflet, and included in the newsletter.
9. Enable information sheets to be posted to young people	An ethics amendment was approved to enable information sheets and consent forms to be posted and/or returned through the mail.
10. Make presentations at local network and Trust meetings	Members of the BRIGHTLIGHT team presented recruitment updates at every available national meeting. Trusts were also informed that the team would come to any local meetings on request. Site specific slides to present at MDTs were provided to all PTCs.
11. First survey to be online or telephone rather than face-2-face	This request could not be accommodated. A single mode of administration had been developed for the first survey.[4]

CWT: Cancer Wait Time database; MDT: multi-disciplinary team; NWCIS: North West Cancer Intelligence Service (after the move to Public Health England became known as the North West Knowledge Intelligence Team). PTC: Principal Treatment Centre; TYAC: Teenagers and Young Adults with Cancer (the organisation representing healthcare professionals working in this area).

[1] Ipsos MORI were the commercial company administering the BRIGHTLIGHT Survey; [2] Ethics guidance in the United Kingdom recommends a minimum of 24 hour between providing information and gaining consent to give participants time to process information; [3] NWCIS sent a monthly email to a dedicated person in each recruiting trust with a list of potentially eligible patients identified through the Cancer Waits dataset as newly starting treatment; [4]Subsequent waves had a choice of online or telephone interviewer administered survey; the online option has only been selected by a minority of young people

BRIGHTLIGHT Cohort profile – supplemental file 2

Supplemental file 2: Method for calculating the TYA Cancer Specialism Scale (TYA CSS) to assign level of care

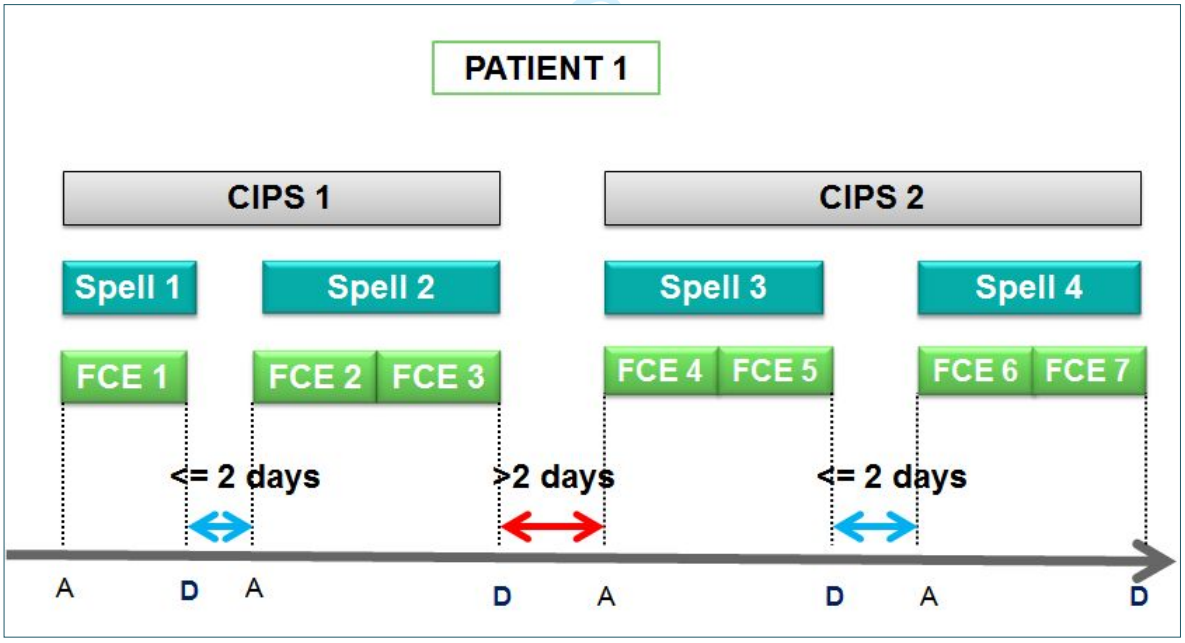
The TYA CSS is derived from admitted patient care data using linked Hospital Episode Statistic (HES) data. HES data from 2011/12 to 2016/17 were obtained from NHS Digital and linked to patients from the BRIGHTLIGHT cohort using the following identifiers: NHS Number, sex and postcode. The method for calculating the TYA CSS is adapted from an approach first proposed by Birch in 2013[1].

Hospital activity within HES is recorded in three ways (Figure 1):

1. Finished consultant episodes (FCEs)
2. Spells (sequential hospital encounters with different consultants)
3. Continuous inpatient spells (CIPS: hospital admissions for the same patient receiving care from different consultants and different providers/trust within two days after discharge)

FCE is the standard measurement unit for hospital activity and considered to provide more accurate estimates of consultant workload and hospital resources[2]. FCE was used for the basis of analysis and derivation of the TYA CSS to ensure we used all available data on consultant care at the deepest level of granularity available.

Figure 1: Different classifications of hospital admission for an example patient based on HES



Abbreviation: FCEs -finished consultant episodes, CIPs -continuous inpatient spells, A-admission, D- discharge.
Source: Analysing Patient-Level Data Using Hospital Episode Statistics (HES), University of York.

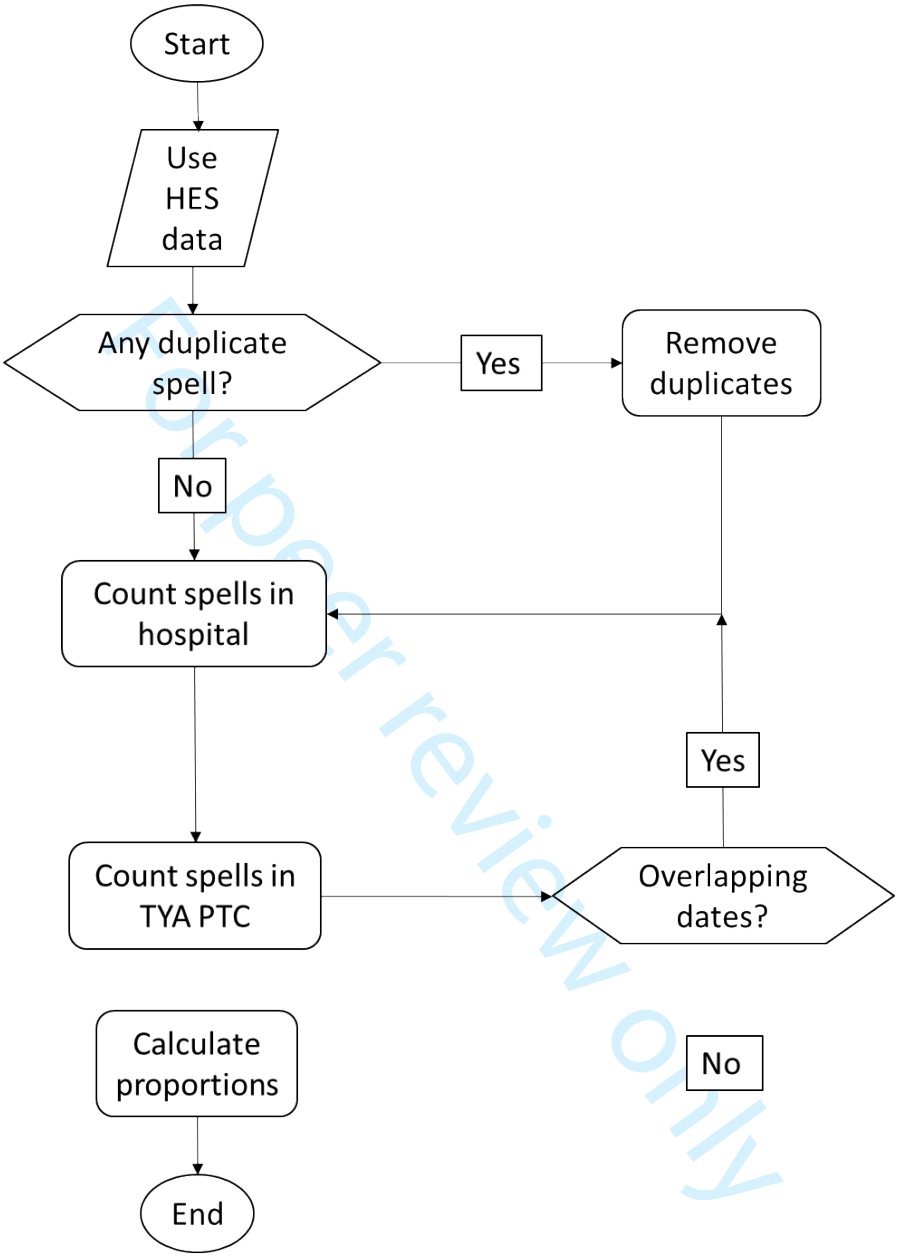
[1] Birch RJ. Teenage and young adult cancer in England – the patient journey and experience. The University of Leeds, PhD Thesis 2013

[2] Hargreaves DS, Viner RM. Adolescent inpatient activity 1999–2010: analysis of English Hospital Episode Statistics data. Archives of disease in childhood 2014; 99: 830-833

BRIGHTLIGHT Cohort profile – supplemental file 2

The development of the TYA CSS is summarised in Figure 2.

Figure 2: Summary of the process for calculating the TYA CSS



Data cleaning

HES data were cleaned to remove duplicates and to clarify some of the diagnostic coding. Reference was made to the HES admitted patient care data dictionary[3] to guide the data cleaning process in order to ensure accuracy and consistency in the recording and analysis of the HES records.

Duplicates were removed to ensure there were not several copies of the same admission being recorded for the same patient. These were identified by ascertaining whether more

[3] HSCIC. HES data dictionary. HEALTH AND SOCIAL CARE INFORMATION CENTRE 2016, 20 January 2016; Available from: http://www.hscic.gov.uk/hesdatadictionary

than one admission began on the same date for a single patient and then cross checking this against admission reasons, procedure codes and treating physician code. Examples of fields which would be indicative of duplicate admission records include multiple HES_IDs, episode start date, episode end date, admission date and discharge date.

Location of specialist care centres

The aim of the study is to evaluate the value of specialist cancer services. 'Specialist' was originally defined in the *Improving Outcomes Guidance (IOG)*[4] as 13 principal treatment centres (PTCs) across England. To account for the age range of the BRIGHTLIGHT cohort starting at 13 years, PTCs also included children's PTCs where the age of admission for the TYA PTC did not include younger adolescents (Table 1). The hospital codes for the look up tables were taken from NHS Digital[5].

Calculation of the scale

The level of specialist care received was calculated from the time of diagnosis (taken from the date recorded in the National Cancer Registration and Analysis Service dataset)

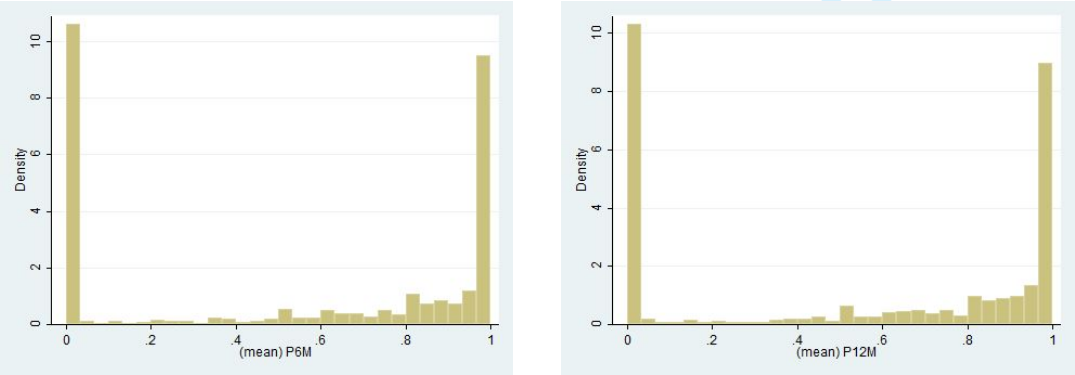
1. Six months after diagnosis: Spells in TYA PTC from diagnosis at 6 months/Total spells from diagnosis at 6 months
2. 12 months after diagnosis: Spells in TYA PTC from diagnosis at 12 months/Total spells from diagnosis at 12 months

For every individual, HES data were used to calculate the number of inpatient and day case bed days spent in a specialist centre (A), as well as the number of total bed days across all secondary care services (B) within the first 6 and 12 months after diagnosis. The proportion of time spent in a specialist centre was then derived as (A)/(B).

Defining the levels of care

Inpatient HES data were successfully linked to 1,074 out of 1,114 young people recruited to BRIGHTLIGHT. The distribution of the proportion of care by 6 months and 12 months after diagnosis suggested there were three natural groups occurring within the data (Figure 3).

Figure 3: Distribution of the proportion of care receive in a TYA PTC



[4] National Institute for Health and Care Excellence. Guidance on cancer services: improving outcomes in children and young people with cancer. NICE, London 2005https://www.nice.org.uk/guidance/csg7/resources/improving-outcomes-in-children-and-young-people-with-cancer-update-773378893 [Accessed 30/08/18]

[5] https://digital.nhs.uk/services/organisation-data-service

BRIGHTLIGHT Cohort profile – supplemental file 2

Table 1: List of principal treatment centres in England (2012-2014) for young people aged 13-24 years

Principal Treatment Centre	**Hospital**
Cambridge University Hospitals NHS Foundation Trust	Addenbrookes Hospital (aged 14-24)
The Christie NHS Trust	Christie Hospital (aged 16-24)
Manchester University Hospitals NHS Foundation Trust	Royal Manchester Children's Hospital (aged 13-15)
Clatterbridge Centre for Oncology NHS Foundation Trust	Clatterbridge Centre (aged 16-24)
Alder Hey Children's NHS Foundation Trust	Alder Hey Children's Hospital (aged 13-19)
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Royal Liverpool Hospital
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Broadgreen Hospital
Leeds Teaching Hospitals NHS Trust	Leeds General Infirmary (aged 13-16)
Leeds Teaching Hospitals NHS Trust	St James's University Hospital (aged 17-24)
Nottingham University Hospitals NHS Trust	City Campus (aged 18-24)
Nottingham University Hospitals NHS Trust	Queens Medical centre (aged 13-18)
Sheffield Teaching Hospitals NHS Foundation Trust	Weston Park Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Royal Hallamshire Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Sheffield Children's Hospital (aged 13-16)
Southampton University Hospitals NHS Trust	Southampton General Hospital (aged 16-24)
Southampton University Hospitals NHS Trust	Southampton Children's Hospital (aged 13-15)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Northern Centre for Cancer Care (aged 19-24)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Royal Victoria Infirmary (aged 13-18)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Sutton (aged 13-24)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Fulham (aged 17-24)
University College London Hospitals NHS Foundation Trust	University College Hospital (aged 13-24)
University College London Hospitals NHS Foundation Trust	Cancer Centre (aged 13-24)
University Hospital Birmingham NHS Foundation Trust	Queen Elizabeth Hospital (aged 16-24)
Birmingham Children's Hospital NHS Trust	Birmingham Children's Hospital (aged 13-18)
University Hospital Bristol NHS Foundation Trust	Bristol Haematology & Oncology Centre (aged 17-24)
University Hospital Bristol NHS Foundation Trust	Royal Hospital for Children (aged 11-16)
University Hospital Bristol NHS Foundation Trust	Bristol Royal Infirmary
University Hospital Bristol NHS Foundation Trust	St Michael's Hospital
University Hospitals of Leicester NHS Trust	Leicester Royal Infirmary (aged 13-24)
Oxford University Hospital NHS Trust	Churchill Hospital (aged 18-24)
Oxford University Hospital NHS Trust	John Radcliffe Children's Hospital (aged 13-18)

BRIGHTLIGHT Cohort profile – supplemental file 3

Supplementary File 3: Development of the BRIGHTLIGHT Severity of Illness Index (BRIGHTLIGHT SIX)

Rationale for developing a bespoke severity index

Within the BRIGHTLIGHT cohort, place of care was not randomly assigned but instead determined by local pathways of care, key influences including the type of cancer, age, proximity to principal treatment centres. As a consequence, differences exist between those who have all/some of their treatment in the teenage and young adult (TYA) Principal Treatment Centre (PTC) and those who have had no care in a TYA PTC. This fundamental difference between the populations of patients who receive no, some or all TYA PTC care was thought likely to be a major confounder in the interpretation of any observed differences in patient experience and outcome between these groups. The differences may not be reflected accurately if cases were grouped solely by, say, tumour type or disease stage due to the considerable variation between tumour types and between similar tumours of different stages in the intensity of treatment received and the likelihood of survival. To interpret the significance of any observed differences in our primary or secondary outcome measures across the populations with no, some or all TYA PTC care, we needed a measure that would allow comparison across patients with different tumours, but capable of discriminating between patient populations. Our primary outcome was quality of life (QOL) and a powerful determinant of QOL is 'the burden of cancer' patients had at diagnosis[1]. We wished to consistently and systematically describe the burden of cancer to assist analysis. The severity of illness index therefore needed to reflect prognosis, disease morbidity (symptoms, physical impact) and treatment morbidity (determined by treatment duration, intensity and anticipated late morbidity burden).

The BRIGHTLIGHT Severity of illness index (SIX)

Constructing the index

All cancer types were compared by symptom burden, treatment burden and prognosis using germ cell tumours as a reference: Stage 1 – very likely to survive, treatment either surgery alone or surgery plus a limited burden of chemotherapy, few if any anticipated late effects of treatment; Stage 2-3 – ~90% survival, many have intensive or multimodality treatment or larger operations, some late toxicity burden; Stage 4 – 50% survival and intensive treatment. Stage 4 we classed as 'most severe' and used this as a reference point to compare odds of survival and treatment burden for other cancers.

Germ cell tumours were chosen as a reference because they are relatively common in the TYA age group, have a range of prognoses from excellent to poor, and treatments have a range of

[1] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

morbidity from surgery alone through to very intensive chemotherapy with both acute and long-term sequelae.

Three clinicians and two BRIGHTLIGHT researchers reviewed all cancer types to consider allocation to one of three severity levels. Survival estimates were based on examination of current or recently completed trial protocols where available and using a recently published comprehensive TYA-specific reference textbook[2]. We evaluated treatment burden using duration and expected toxicity from multiple sources, including clinical experience, trial protocols, a current TYA oncology text book and international guidelines (such as the National Comprehensive Cancer Network). In addition, other potentially comparable clinical severity scales were sought from the literature to determine comparability or utility in this context.

Content validity of the index

Once a preliminary scale had been constructed, its content was tested by expert review. At least two additional clinicians with specialist clinical expertise were approached to review each tumour type. The reviewers were sent a short document outlining the purpose of the scale and its development to that point as well as the scale itself. They were interviewed either face-to-face or by telephone by a senior clinician and BRIGHTLIGHT researcher (JSW) and asked to respond to two questions:

1. *Within the row(s) of the cancer types in which you have particular expertise (e.g. central nervous system tumours), do you agree with the allocation of grades of severity?*
2. *Looking at other tumour types, by comparison with other rows, do you agree with the allocation of grades of severity?*

Interviews were recorded and field notes taken. The scale was adjusted in response to expert comments to produce a final version (main paper, Table 2).

Applying the BRIGHTLIGHT SIX

BRIGHTLIGHT researchers (RMT, LAF, DS) independently allocated a severity level to each patient, conducting these assessments blind to responses to the survey, including QOL results. Comparisons between the three scores were made and, where there were differences, adjudication through a fourth researcher (JW) determined whether this was an error or due to ambiguity in the Index.

Other measures of severity

We found only one other example in which investigators had categorised TYA by cancer severity. Husson et al[1] used expected 5-year survival to divide patients into three groups, those with expected survival of greater than 80%, 50-80% and less than 50%.[3] Using the same source

[2] Bleyer, Barr, Ries, Whelan, Ferrari eds. Cancer in Adolescents and Young Adults. Springer International Publishing, Switzerland 2017

[3] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

BRIGHTLIGHT Cohort profile – supplemental file 3

data[4], we also allocated each patient from the BRIGHTLIGHT cohort a second severity level based on 5-year survival.

We compared this method (Five year survival index, FYX) with BRIGHTLIGHT SIX. As anticipated, those judged to have the most severe cancer by BRIGHTLIGHT SIX are distributed across the three survival categories though weighted towards the two lower survival groups. Similarly, most but not all of those with the least severe cancer by BRIGHTLIGHT SIX had the best expected survival. Those with intermediate severity cancer are spread across the three FYX groups (Table 1).

Table 1: Comparison between the Five year survival Index (FYX) and BRIGHTLIGHT Severity of Illness Index (SIX)

	SIX level		
FYX	Least	Intermediate	Most
<50%	1	100	71
50-80%	56	98	171
>80%	546	56	7

We then analysed survival of the BRIGHTLIGHT cohort using the two indices. Figure 1 demonstrated a clear discrimination in survival by BRIGHTLIGHT SIX, consistent with anticipated survival being an important but not sole component of the index. The survival of the BRIGHTLIGHT cohort was then examined by allocated FYX category (Figure 2). FYX failed to distinguish three groups with distinct survival as that of those allocated to the two lower categories was superimposed.

[4] Bleyer, A. (2011). "Latest Estimates of Survival Rates of the 24 Most Common Cancers in Adolescent and Young Adult Americans." J Adolesc Young Adult Oncol 1(1): 37-42.

BRIGHTLIGHT Cohort profile – supplemental file 3

Figure 1: Survival by BRIGHTLIGHT Severity of Illness Index

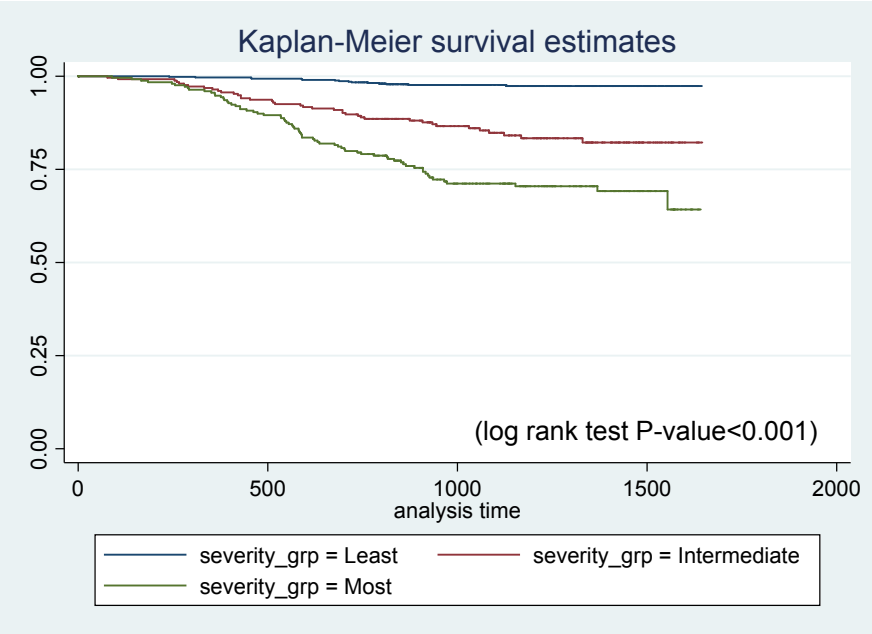
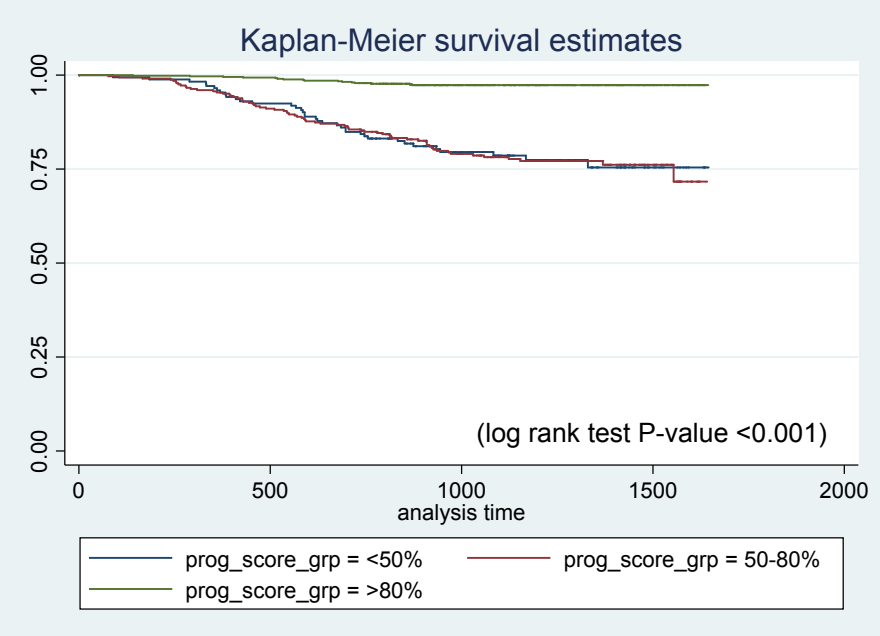


Figure 2: Survival of BRIGHTLIGHT cohort against allocated FYX group



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Description of the BRIGHTLIGHT Cohort: the longitudinal evaluation of teenagers and young adult cancer services in England

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Keywords:	BRIGHTLIGHT, Recruitment, Teenagers and Young Adults, Cancer, Observational Research, Cohort

AFTER REVIEW

Description of the BRIGHTLIGHT Cohort: the longitudinal evaluation of teenagers and young adult cancer services in England

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ABSTRACT

Objective: International recognition of the unique needs of young people with cancer is growing. Many countries have developed specialist age-appropriate cancer services believing them to be of value. In England, 13 specialist Principal Treatment Centres (PTC) deliver cancer care to young people. Despite this expansion of specialist care, systematic investigation of associated outcomes and costs has to date, been lacking. The aim of this paper is to describe recruitment and baseline characteristics of the BRIGHTLIGHT cohort, and the development of the bespoke measures of levels of care and disease severity, which will inform the evaluation of cancer services in England.

Design: Prospective, longitudinal, observational study.

Setting: Ninety-seven NHS hospitals in England.

Participants: A total of 1,114 participants were recruited diagnosed between July 2012 and December 2014: 55% (n=618) male, mean age was 20.1 years (SD=3.3), most (86%) were white and most common diagnoses were lymphoma (31%), germ cell tumour (19%) and leukaemia (13%).

Results: At diagnosis, median quality of life score was significantly lower than a published control threshold (69.7 points); 40% had borderline-severe anxiety, and 21% had borderline-severe depression. There was minimal variation in other patient-reported outcomes according to age, diagnosis or severity of illness. Survival was significantly worse in the Cohort than for young people diagnosed during the same period who were not recruited (cumulative survival probability 4 years after diagnosis: 88% vs. 92%).

Conclusions: Data collection was completed in March 2018. Longitudinal comparisons will determine outcomes and costs associated with access/exposure to PTCs. Findings will inform international intervention and policy initiatives to improve outcomes for young people with cancer.

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Strengths & limitations of this study

5 bullet points

- This is the largest ever prospective cohort of young people with cancer, examining not only cancer outcomes but also the social and educational impact of a cancer diagnosis.
- The socio-demographic characteristics of the cohort are broadly similar to the contemporary total teenage and young adult cancer population thus increasing the generalisability of results.
- Data has been collected from multiple sources, results therefore reflect the perspective of the patient, plus clinical care and data on health service use.
- Study results will provide new information on cancer in young people and determines if access to a Principal Treatment Centre adds value; the relationships between specialist care and outcomes have previously been unclear. Findings will contribute to intervention and policy efforts to improve outcomes and patient experience for young people with cancer
- The cohort comprises 20% of young people diagnosed with cancer during the time period. A decrease from original target sample size (n=2,012) consequent of recruitment difficulties has resulted in a reduced statistical power to address the potential impact of heterogeneity within the cohort.

INTRODUCTION

BRIGHTLIGHT is a programme of research which aims to determine whether specialist care for teenagers and young adults (TYA) with cancer is associated with improved outcomes. The National Institute for Health and Care Excellence (NICE) outlined in the *Improving Outcomes Guidance for children and young people with cancer* [1] a model of specialised care based on a limited number of hospitals designated as principal treatment centres (PTC). At that time minimal information was available about either the constituent parts of such specialist care or the benefits that might accrue from it and why. BRIGHTLIGHT comprises six interlinked projects centred upon a prospective, longitudinal cohort of young people recruited soon after a diagnosis of cancer that examines their outcomes and experiences of cancer care. Additional studies address elements of specialisation; the environment of care [2, 3]; the competencies desirable in healthcare professionals delivering specialist care [4]; a metric to quantify specialist care; caregiver's experience of care; and a health economic analysis to determine the cost of specialist care. The programme has been underpinned by an extensive patient and public involvement strategy [5-9].

Cancer in young people is uncommon, accounting for less than 1% of all new cancer diagnoses in England [10]. Despite its rarity, cancer is the second leading cause of death for young people, accounting for 11% of deaths in those aged 15-24 years [11, 12]. In addition, a number of issues argue for special attention for young people with cancer and for robust evidence to support current and future healthcare policies. For example, young people present with a spectrum of cancer types that is distinct from those affecting younger children and older adults [11]. A cancer diagnosis during adolescence and young adulthood has an acute and unique impact on this critical and complex stage of life development, disrupting physical health, social and educational goals as well as psychological wellbeing [13]. These

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factors have additional importance when considered against the advantages which accrue to society from the successful treatment through the prolonged fulfilment of their contribution in employment and other societal impacts [14].

While most young people are cured, outcomes for some cancers have not improved in line with those achieved for children and older adults [15]. There exists a general consensus among healthcare professionals that the needs of young people are poorly met by cancer services that are tailored towards the needs of children and older adults [16]. Young people fall between child and adult cancer services, into what has been described as either 'the grey zone' [17] or 'no man's land' [18]. Prolonged routes to diagnosis, unfavourable tumour biology with increasing age, limited access to clinical trials, lack of compliance with treatment protocols, inconsistent use of molecular diagnostics that may assist with optimal care, and a lack of specialist supportive care have all been implicated in the short fall in survival improvements [19-28].

Young people themselves have described unsatisfactory experiences of care which include: lack of recognition of their autonomy; failure to facilitate them to meet normal life goals during treatment; lack of peer support; care by staff with little experience of young people; and finally, inappropriate care environments [9, 29-31]. The inability of traditional healthcare silos to meet the unique psychosocial and healthcare needs of this specific population is increasingly highlighted [32-34]. Place of treatment and delivery of cancer care, in terms of both disease and age-appropriate specialist settings is increasingly acknowledged as potentially significant to the outcomes for young people with cancer [35, 36].

To address these unique needs and deficit in outcomes' knowledge, in August 2005 the NICE *Improving Outcomes Guidance* recommended that all care for patients under 19 must be provided in age-appropriate facilities and those aged 19 and over should have 'unhindered access to age-appropriate facilities and support when needed' [1]. To accommodate this recommendation thirteen TYA PTCs were identified across England. Key components of the services of the TYA PTC encompass tumour site-specific expertise delivered in conjunction with meeting the broader psychosocial needs of young people to support successful navigation of critical life transitions. This is directed through the TYA multi-disciplinary team (MDT) [1]. But, despite national guidance supporting this approach to the delivery of cancer care for young people aged 15-24 years [1]. around half of young people continue to be treated in children's and adult cancer units with no or limited access to the TYA PTC, many receiving care in hospitals 'designated' by NHS commissioners to provide elements of specialist care that are available in a TYA PTC.

The aim of the BRIGHTLIGHT programme of research is to evaluate the benefit of specialist TYA cancer services for young people aged 13–24 years. The study has four key objectives specific to the cohort:

1. Relate the proportion of care young people received in a TYA PTC to: quality of life, satisfaction with care, clinical processes and clinical outcomes
2. Examine young people's experience of cancer care through a longitudinal descriptive survey
3. Compare social and educational milestones amongst young people receiving different levels of TYA cancer care
4. Determine the costs of specialist care to young people, their families and the NHS

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Objectives

The aim of this paper is to describe the complex recruitment process for establishing the BRIGHTLIGHT cohort, provide details of bespoke measures of levels of care and disease severity that were developed to inform the analysis of the evaluation, and to describe the baseline characteristics of the cohort.

STUDY DESIGN

The BRIGHTLIGHT cohort is a prospective longitudinal cohort study, obtaining data through a bespoke survey, administered through face-to-face interview, telephone interview and online, five times over three years: 5-7 months after diagnosis then at 12, 18, 24 and 36 months [37].

PATIENT AND PUBLIC INVOLVEMENT

The focus of this study was identified by young people as a priority area for research. BRIGHTLIGHT was preceded by a period of feasibility work where we worked with young as co-researchers to develop the research questions, outcome measures and study design [6, 9]. the study has a Young Advisory Panel who have worked with us since 2011, who have been integral in naming the study [5], study management [7, 8], identifying other areas for research [38] and dissemination [39].

SAMPLE AND SETTING

Participants

The BRIGHTLIGHT cohort included young people aged 13-24 years, newly diagnosed with cancer (ICD-10 codes C00-C97) in an English hospital and recruited within four-months of diagnosis between July 2012 and March 2015. Eligibility criteria were as inclusive as possible so no restriction according to language or a sensory impairment that affected communication was applied. The only exclusion criteria were: young people receiving a custodial sentence; if the young person was not anticipated to be alive at the first point of data collection (6-months after diagnosis); recurrence of a previous cancer or they were not capable of completing a survey, e.g. sedated and in intensive care.

Recruitment

Young people present with a wide range of cancer diagnoses [11]. It was anticipated that to identify and recruit potentially eligible patients would be the biggest challenge because of: 1) low incidence 2) presenting to numerous points in healthcare system, due to age and multiple diagnostic subtypes; and 3) inconsistent referral pathways for tertiary care. The NICE guidance was issued in 2005 [1], and by 2010 only 40% of newly diagnosed young people were known to a TYA MDT based at a PTC [40]. Analysis of the national cancer datasets between 2010 and 2011 indicated that young people were being treated in an additional 133 hospitals across England. Thus, to capture the full cohort of young people we needed to open recruitment in as many hospitals as possible, have a mechanism to identify young people across the country and also have access to an extensive network of researchers to recruit and administer the study questionnaires.

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There were two mechanisms for identifying young people: first through the national Cancer Waiting Times (CWT) dataset, which has been reported in detail previously [41]. This is routinely collected NHS data used to monitor diagnostic and treatment targets; feasibility work suggested young people could be identified within three months of diagnosis [42]. However, when this method was applied nationally it was found to be neither timely nor accurate so a second mechanism was introduced: Principal Investigators were asked to liaise with the coordinators of all tumour-specific MDTs (except prostate cancer) so the person managing recruitment to the study could be informed of new diagnoses in young people aged 13-24 years. A third method to directly approach young people to invite them to participate was also introduced in the later stages of recruitment but did not significantly impact on accrual [43].

The second challenge was working with a very large number of hospitals, of which most were likely to identify a few eligible patients over the course of the study and who might present to one of several departments. BRIGHTLIGHT opened to recruitment in 109 hospitals, of whom 97 identified and recruited between 1-106 (median 5) young people per hospital, 12 not recruiting any participants. England has a national network of research personnel funded by the National Institute for Health Research (NIHR), tasked with facilitating recruitment into clinical studies [41]. The aim was to recruit 2,012 young people diagnosed between July 2012 and December 2013. Despite making multiple targeted amendments to the protocol and iteratively working with NIHR researchers and the TYA healthcare professional community to increase the proportion of patients who were offered study entry (supplemental file 1), recruitment was slower and lower than anticipated. In April 2014, an extension to recruitment until April 2015 was approved (young people diagnosed until December 2014, recruited within 4 months of diagnosis), and a lower target sample size was agreed (Figure 1).

Ethical approval and consent

The study was approved by London Bloomsbury NHS Research Ethics Committee (reference LO/11/1718). Approval by the Secretary of State under Regulation 5 of the Health Services (Control of Patient Information) Regulation 2002 was obtained from the Health Research Authority Confidentiality Advisory Group (reference ECC 8-05(d)/2011) to access the CWT dataset, Hospital Episode Statistic (HES) data and data from the National Cancer Registration and Analysis Service (NCRAS).

METHODS

Data were collected from three sources: young people, patient medical records, and central NHS and Public Health England (PHE) databases.

Data from young people

Patient-reported outcomes were collected from young people at five time points over three years: 4-7 months after diagnosis (wave 1), 12 months (wave 2), 18 months (wave 3), 2 years (wave 4) and a final data capture 3 years after diagnosis (wave 5). Data were collected using a study-specific questionnaire, the BRIGHTLIGHT Survey [37] (available under licence from https://xip.uclb.com/i/healthcare_tools/brightlight_wave1.html), which was administered as a face-to-face interview in young people's homes at wave 1. Subsequent

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waves were administered online or through telephone interviews. At wave 1, young people also completed study-specific health economics questionnaires, described below.

The BRIGHTLIGHT Survey

The BRIGHTLIGHT Survey is an investigator and young person-designed self-report questionnaire that was administered through computer-assisted personal, telephone or web interviewing or web by an independent research organisation. It was developed utilising patient-experience literature [44] and was underpinned by a conceptual framework to guide question content [9]. The BRIGHTLIGHT Survey contains five validated outcome measures and questions to reflect young people's experience of diagnosis and cancer care (Table 1) [37]. Completion of treatment occurs at different time points according to diagnosis. During the feasibility work young people emphasised that they did not want to be asked questions about cancer when treatment ended and therefore the computer administration of the BRIGHTLIGHT Survey had complex routing to ensure young people were only asked questions that were relevant to their current situation [37]. For example, questions related to pre-diagnosis and diagnostic experience were only asked at wave 1. The BRIGHTLIGHT survey also utilised 'pull through' options so that participants could reflect on responses given in previous waves before answering. For example, questions about employment/education goals were tailored so participants could be asked again at wave 5 to ascertain if goals had changed and if this was cancer-influenced.

Table 1: Summary of the content of the BRIGHTLIGHT Survey

Construct and questionnaire	Details
Quality of life – Pediatric Quality of Life Questionnaire (PedsQL™) [45]	Contains 23 items scored on a 5-point Likert scale. Four domains: physical, emotional, social and work/school functioning. Two summary scores (physical and psychosocial function) and a total score. Domain, summary and total scores on 0-100 scale, with 100 representing the best possible quality of life. Scores <69.7 indicate a high risk of impaired quality of life [46].
Health status – Euroqol- 5 Dimension 3 level (EQ-5D-3L) [47]	Comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) scored on 3 levels (no, some, severe problems). The EQ visual analogue scale records self-reported health on a vertical scale ranging from 'best imaginable health state' to worst imaginable health state'. Scores 0-1 with 0 representing death and 1 perfect health (negative scores represent a health state worse than death).
Anxiety and depression – Hospital Anxiety and Depression Scale (HADS) [48]	A measure of depression and anxiety. Contains 14 items, scored on a four-grade scale (0 to 3). Summary scores for depression and anxiety (ranging from 0 to 21). Scores of 8-10 are defined as borderline and 11 and over are considered moderate/severe anxiety and depression [49].
Social support - Multi-dimensional Scale of Perceived Social Support (MSPSS) [50]	Scores for support by friends, family and significant others plus total support score. Contains 12 statements, rated on 7-point Likert scale. Total support score is an average ranging from 1-7, sub-support

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	scores range 4 – 28. Total scale score 1-2.9 are considered low support; a score of 3-5 is considered moderate support; and scores from 5.1-7 are considered high support.
Illness perception - The Brief Illness Perception Scale (BIPS) [51]	Measures the emotional and cognitive representations of illness. Contains eight* questions with fixed response scale specific for each question, e.g. not at all – extremely helpful. Each question represents a different dimension of illness perception: consequence, personal control, treatment control, timeline, identity, coherence, emotional representation, concern. Responses scored 1 – 10, the higher the score the greater perceived illness impact. No overall score and each question represents a single domain.
Cancer experience questions [37]	Comprises of 12 experience domains: pre-diagnosis experience, diagnostic experience, place of care, contact with healthcare professionals, treatment experience, fertility, involvement in clinical trials, adherence, communication and coordination of care, education, employment, wellbeing and relationships. Total of 238 questions with question specific responses describing experience

*Timeline statement not included

Health economics questionnaires

Cancer/treatment related costs incurred by young people and families were collected using a study-specific Cost of Care Questionnaire and Cost Record. These included questions regarding: travel (car parking, petrol and capital depreciation, public transport); time off work; medical equipment use; prescription and over the counter drug use; cost of accommodation incurred through hospitalisation; complementary and alternative medicine; and cost of family care for siblings. The Cost of Care Questionnaire was administered at wave 1 and required young people and their families to record costs incurred from the above items retrospectively since diagnosis. The Cost Record was given at waves 1 and 2, requesting the same information collected prospectively, on a weekly basis.

Data from medical records

Research teams who recruited young people completed an electronic Case Report Form (CRF) 12 months after diagnosis, which contained key variables relating to diagnosis, treatment, clinical process and outcome variables. This included postcode at the time of diagnosis, locations of care, details of diagnosis, MDT treatment planning and care, and outcomes at 12 months after diagnosis. The Index of Multiple Deprivation (IMD) is a measure of socioeconomic status [52] and was derived from the postcode at diagnosis, based on the population denominator of England. Clinical processes of care were defined as *documentation of*:

1. Histological diagnosis
2. Molecular diagnosis
3. Cancer stage or prognostic group
4. Initial treatment plan
5. Evidence of multidisciplinary communication

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6. Assessment by supportive care services, defined as documented contact with a Clinical Nurse Specialist plus one other member of the MDT (social worker, youth support coordinator, counsellor, psychologist, dietician, physiotherapist, occupational therapist)
7. Fertility discussion
8. Consideration for inclusion in a clinical trial

Data from national datasets

Data from NCRAS and HES were used to supplement and validate details of treatment received in the TYA PTC, to support a detailed health economic evaluation based on hospital attendance and healthcare received, and to cross check against the e-CRF. NCRAS data included date of diagnosis, tumour morphology, staging and treatment data; and HES data included dates for admitted patient care (APC), outpatient and accident and emergency attendance, plus receipt of chemotherapy and radiotherapy.

DEVELOPMENT OF BESPOKE METRICS

Defining levels of care

BRIGHTLIGHT aims to evaluate exposure to specialist TYA cancer services, defined as treatment in the TYA PTC. In recognition that patients may receive elements of care in more than one hospital, we proposed that care could be categorised by three levels according to the proportion of care received in a TYA PTC. To accurately allocate cohort participants to the appropriate level of care, analysis of HES data were used. In summary, PTC Trust codes were identified for 2012-2014 and applied to HES data so the proportion of days spent in a TYA PTC in the first 6 months and 12 months after diagnosis could be calculated (details provided in supplemental file 2).

Defining severity of illness

Advanced cancer is associated with poorer quality of life [53, 54]. We planned to compare quality of life of those treated in different care environments. To do so, we needed to consider ways to control for differences between patients which might influence this outcome and in particular, the severity of their cancer. However, this is difficult for TYA as they present with a heterogeneous array of malignancies [11]. While most cancers have staging criteria which differentiate between more or less extensive disease (typically groups 1-4 in ascending order of worsening survival), stage is not directly comparable between cancer types and a comparison based purely on staging would be meaningless due to the variation in outcomes between different cancers allocated to the same stage level. For example, stage 4 thyroid cancer is associated with a much higher chance of survival than say, stage 4 bowel cancer. Furthermore, survival alone is a good indicator of severity of illness as it takes no account of disease and treatment morbidity both for the short and long term. We therefore developed a bespoke 'severity' grading system to include symptom and treatment burden as well as predicted survival and burden of late effects. Each cancer type was graded as least, intermediate and most severe based on cancer-specific information thus allowing comparisons between groups of patients with multiple types of cancer (Table 2; detailed methodology is presented in supplemental file 3).

ANALYSIS

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The number of young people at each stage of the project were described using a flow diagram, including the numbers eligible, consenting to be involved, and followed up at each survey point. Reasons for non-participation at each stage were summarised. Potentially eligible patients who did not participate in the cohort study were compared against those who consented with regard to age, gender, ethnicity, location (based on the network linked to each PTC) and diagnosis. Data in both groups were summarised as means with standard deviations (sd), medians with interquartile ranges (IQR) or frequency and percentage (%), as appropriate and comparisons made using standard Chi squared and t-tests. Since sample sizes for these comparisons were very large, statistical significance is defined as $P<0.001$. Survival from diagnosis was summarised using Kaplan Meier plots and the cohort and non-cohort groups compared using Cox regression to adjust for age, gender, ethnicity, location and type of cancer. Patient reported outcomes collected in the first wave were scored according to published guidance for each of the validated measures. The characteristics of the cohort were summarised using means/medians (sd/IQR) or frequency (%) as appropriate.

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Table 2: BRIGHTLIGHT Severity of Illness Index (see supplemental file 3)

Cancer type [11]	**Least severe**	**Intermediate severity**	**Most severe**
Germ cell tumours	Stages 1-3; Stage unknown	Stage 4 (stage 1S=stage 4)	
Leukaemias	CML	ALL; Other and unspecified	AML
Non-Hodgkin lymphoma and non-specified lymphoma	Over 16yrs, protocol unknown Stage 1-2	Over 16s, protocol unknown; Stage 3-4; Any paediatric-type protocol; All unknown	Burkitts (ICD10 C83.7, morphology code 9687/3)
Hodgkin lymphoma	All stages		
Central nervous system tumours	Pituitary adenomas (D35.2); Sub-ependymal giant cell astrocytoma (C43.2)	Other completely resected WHO grade I tumours for which surgery is the only treatment needed - except craniopharyngiomas	Craniopharyngiomas; incompletely resected or unresectable grade I tumours; all grade II-IV tumours, any needing radiotherapy or chemotherapy. This includes ependymomas, medulloblastomas and intracranial GCTs
Bone tumours	Surgery only (low grade, periosteal, parosteal)		All other
Soft tissue sarcoma	Stages 1-2	Stage 3; Unknown	Stage 4
Rhabdomyosarcoma	Low risk EpSSG A-D[1]		All others; Unknown
Melanoma	Stages 1-2 (except 2c)	Stage 2c; Stage 3 (except 3c); Stage unknown	Stage 3c; Stage 4
Carcinoma	All thyroid; All Stage 1; Cervix stage unknown	Stages 2-3; All nasopharyngeal; Stage unknown (except cervix)	Stage 4
Miscellaneous and unspecified		All	

[1] EpSSG: European Paediatric Soft Tissue Sarcoma Study Group

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RESULTS

A total of 1,126 young people were recruited for whom valid consent was available from 1,114 (Figure 2). Recruiting hospitals were required to keep a screening log, which was returned to the BRIGHTLIGHT team by 95 (87%) hospitals when recruitment ended. Of the 2,900 young people who had been screened, 429 (15%) were reported as not being eligible and 1,877 (65%) were eligible to participate. No details were provided for the remaining 594 (20%). Only 426 (23%) of those eligible had refused to participate, which was lower than the 35% we had anticipated and accounted for [8]. Of the 15% recorded as being ineligible, just over half (225, 52%) had either no reason recorded or appeared to have been deemed to be ineligible incorrectly.

Data were obtained from NCRAS for young people diagnosed in the same time period, who were potentially eligible, i.e., alive 6-months after diagnosis and place of residence was not linked to a prison postcode. A total of 5,953 young people were diagnosed with cancer between July 2012 and December 2014, of whom 5,835 (98%) were potentially eligible to participate[1]; 1,114 (19%) appeared in the BRIGHTLIGHT Cohort.

Clinical and NHS data were available for all 1,114 young people. Of these, 830 (75%) completed the wave 1 survey (Figure 2). In total, 163 (20%) participated once, 186 (22%) twice, 195 (24%) completed three, 173 (21%) completed four and 113 (14%) took part in every wave.

Non-participants were similar in age and ethnicity to those in the BRIGHTLIGHT cohort but there were differences in gender (a lower proportion of males in non-participants) and inclusion by tumour type (a greater proportion of young people with leukaemia and lymphoma, germ cell tumours and bone tumours compared to non-participants but lower representation of brain tumours, skin cancers and carcinomas) (Table 3).

Table 3: Comparison of characteristics of participants and non-participants

		N	BRIGHTLIGHT Cohort	N	Non-Participants	P-values[3]
Age at Diagnosis (years)	Mean (SD) Median (IQR)	1114	20.13 (3.28) 20.64 (17.58, 22.95)	4721	19.94 (3.33) 21 (17, 23)	0.08
Gender	Male Female	1114	618 (55%) 496 (45%)	4721	2213 (47%) 2508 (53%)	<0.0001
Ethnicity	White Asian Black Chinese Mixed Other	1085	936 (86%) 82 (8%) 22 (2%) 4 (<1%) 26 (2%) 15 (1%)	4316	3643 (84%) 288 (7%) 156 (4%) 34 (<1%) 74 (2%) 121 (3%)	0.002
Type of cancer[1]	Leukaemia Lymphoma CNS Bone	1114	145 (13%) 350 (31%) 46 (4%) 102 (9%)	4721	300 (6%) 781 (17%) 735 (16%) 177 (4%)	<0.0001

[1] 109 young people died within 6-months of diagnosis so were assumed to be too sick to be approached and nine were in prison.

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	Sarcomas		78 (7%)		207 (4%)	
	Germ cell		212 (19%)		504 (11%)	
	Skin		45 (4%)		709 (15%)	
	Carcinoma (not skin)		125 (11%)		1210 (26%)	
	Miscellaneous specified		9 (<1%)		55 (1%)	
	Unspecified malignant		2 (<1%)		43 (1%)	
Geographical location[2]	Birmingham	1114	155 (14%)	4618	459 (10%)	<0.0001
	Bristol		116 (10%)		351 (8%)	
	Cambridge		23 (2%)		276 (6%)	
	Manchester		103 (9%)		391 (8%)	
	Merseyside		42 (4%)		239 (5%)	
	East Midlands		135 (12%)		278 (6%)	
	Leeds		106 (10%)		254 (6%)	
	Newcastle		59 (5%)		305 (7%)	
	Oxford		19 (2%)		249 (5%)	
	London (south)		77 (7%)		668 (14%)	
	Sheffield		37 (3%)		174 (4%)	
	Southampton		83 (8%)		221 (5%)	
	London (north)		159 (14%)		753 (16%)	

CNS: central nervous system; SD: standard deviation; IQR: interquartile range

[1] Based on the Birch classification [11]

[2] Hospitals mapped to the multidisciplinary team at the Teenage and Young Adult Principal Treatment Centre they were linked to

[3] P-values from Chi squared tests and t-tests as appropriate.

Of the 1,114 young people in the BRIGHTLIGHT cohort, 618 (55%) were male, mean age at diagnosis was 20.13 years (SD 3.28) and 936 (86%) identified themselves as white. Lymphoma was the most common cancer type (n=350; 31%), followed by germ cell tumours (n=212; 19%) and leukaemia (n=145; 13%) (Table 3). Table 4 details the sociodemographic and clinical characteristics of the BRIGHTLIGHT cohort. There was an even distribution across socioeconomic groups. Most were single (n=606; 84%) and employed or in education (n=531; 64%). Systemic anti-cancer therapy was the most common form of treatment, used for 880 (79%). Thirty (3%) young people received no treatment, just active monitoring. The clinical processes that were most frequently documented in the clinical records were MDT communication (n=1037; 97%), cancer stage or prognostic group (n=1015; 94%), histology (n=974; 91%) and initial treatment plan (n=974; 91%). One hundred and sixty seven (20%) young people reported having a pre-diagnosis long-term condition.

Table 4: Socio demographic and clinical characteristics of the BRIGHTLIGHT Cohort

Characteristic		Number	%
Socioeconomic status (IMD quintile) (N=1088)	1 – most deprived	250	23
	2	194	18
	3	209	19
	4	230	21
	5 – least deprived	205	19
Marital Status (wave 1; N=725)	Married/civil partnership	26	4
	Cohabiting	93	13
	Single/divorced	606	84
Current status (at wave 1; N=830)	Working full/part time	257	31
	In education	274	33

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	Other work (apprentice/intern/voluntary)	17	2
	Unemployed	31	4
	Long term sick	126	15
	Not seeking work	125	15
Length of inpatient stay over 12 months (N=1070) days	Median (IQR)	25	9 to 74
Treatment (N=1114)[2]	Systemic anti-cancer therapy	880	79
	Radiotherapy	324	29
	Surgery	551	50
	Active monitoring	30	3
	Transplant (stem cell or bone marrow)	28	3
Severity of illness (N=1114)	Least	611	55
	Intermediate	254	23
	Most	249	22
Clinical processes of Care (documentation available in clinical records)	Histological diagnosis (n=1072)	974	91
	Molecular diagnosis (n=737)[3]	258	35
	Cancer stage or prognostic group (n=1078)	1015	94
	Initial treatment plan (n=1071)	974	91
	MDT communication (n=1074)	1037	97
	Assessment by supportive care services (n=1057)	563	53
	Fertility being discussed (n=1063)	693	65
	Consideration into a clinical trial (n=1057)	676	64

CNS: central nervous system; IMD: Index of Multiple deprivation; IQR: interquartile range

[1]Based on period of 12 months from diagnosis. Missing for 70 participants: 26 had no days in hospital after diagnosis (inpatient stay was before diagnosis date) and data were missing for 44

[2] N greater than 1114 reflects multiple treatment modalities for some diagnoses

[3] Where relevant, indicated as not relevant in 320

A total of 124 (11%) young people in the BRIGHTLIGHT cohort died before 31st December 2016. Results from Cox regression indicate that a survival benefit for non-BRIGHTLIGHT patients was maintained even after adjustment for age, gender, ethnicity and type of cancer; the risk of death was 34% higher for those in the BRIGHTLIGHT cohort compared with those not in the cohort. (Figure 3; hazard ratio estimate 1.34 (95% confidence intervals 1.09-1.68), p=0.01). There was no evidence that survival of cohort participants compared with non-participants differed by cancer type (P-value for interaction P=0.12).

A summary of patient-reported outcomes recorded at wave 1 are presented in Table 5. Mean total quality of life, physical and emotional domains scores were <69.7 indicating young people were at high risk of impaired quality of life shortly after diagnosis [46]. Forty percent of young people could be classified as 'cases' for anxiety and 22% for depression (borderline-severe) [49]. Young people reported high levels of support from friends (Multi-dimensional Scale of Perceived Social Support cut off >5) and moderate support from family and significant others (score 3-5) [50]. The Brief Illness Perception Scale results indicate that young people felt cancer had a moderate effect on their life but they perceived that treatment was extremely helpful. They perceived themselves as having experienced a moderate number of symptoms and believed they had a good understanding of their cancer. The majority rated their satisfaction with care as being excellent/good (n=777; 94%). Those aged 19-24 years seemed to have better physical and psychosocial quality of life compared to those aged 13-18 years at diagnosis. This older age group also reported more anxiety, lower

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social support, better perceived personal control but lower perceived emotional representation and concerns. According to diagnosis, young people with a solid tumour had better physical scores, perceptions of consequences and identity but less support from friends than those with a blood cancer. Finally, there was a noticeable trend for better total quality of life, physical and psychosocial scores for those with less severe disease and worse emotional score for the intermediate severity group. Young people with less severe disease had better perceived consequences and identify but satisfaction with care was highest in those with the most severe disease.

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Table 5: Summary of the wave 1 patient-reported outcomes

			Age		Diagnosis		Severity of illness		
Characteristic	**N**	**All patients N=830**	**13-18yrs N=302**	**19-24yrs N=528**	**Haematology N=373**	**Oncology N=457**	**Least N=461**	**Intermediate N=194**	**Most N=175**
PedsQL - mean (SD)									
Total score	829	66.20 (19.79)	64.14 (18.53)	67.39 (20.40)	64.59 (18.28)	67.52 (20.86)	70.67 (18.86)	61.55 (19.77)	59.57 (19.25)
Physical summary score	828	59.45 (27.72)	54.67 (26.75)	62.20 (27.91)	56.96 (25.04)	61.47 (29.58)	67.65 (25.49)	52.67 (26.63)	45.33 (26.95)
Psychosocial summary score		80.38 (18.45)	77.88 (18.27)	81.82 (18.42)	79.37 (18.49)	81.21 (18.41)	84.15 (16.75)	75.90 (19.82)	75.43 (18.98)
Emotional summary score		67.64 (22.76)	70.94 (21.83)	65.75 (23.07)	67.75 (21.68)	67.55 (23.62)	68.05 (23.09)	64.92 (23.15)	69.57 (21.21)
EQ-5D – mean (SD)	830	0.76 (0.24)	0.75 (0.23)	0.77 (0.24)	0.77 (0.22)	0.76 (0.25)	0.81 (0.21)	0.71 (0.26)	0.71 (0.24)
Total score									
- **median (IQR)**		0.80 (0.69-1)	0.80 (0.62-1)	0.81 (0.69-1)	0.80 (0.69-1)	0.80 (0.66-1)	0.85 (0.73-1)	0.73 (0.62-1)	0.75 (0.59-0.88)
HADS – mean (SD)[1]	830								
Anxiety score		6.89 (4.39)	6.14 (4.12)	7.32 (4.49)	6.79 (4.36)	6.98 (4.43)	7.23 (4.55)	7.01 (4.44)	6.14 (3.83)
- Borderline n (%)		160 (19%)	51 (17%)	109 (21%)	75 (20%)	85 (19%)	82 (18%)	44 (23%)	34 (19%)
- Moderate/severe n (%)		172 (21%)	48 (16%)	124 (23%)	70 (19%)	102 (22%)	106 (23%)	40 (21%)	26 (15%)
Depression score		4.62 (3.68)	4.45 (3.38)	4.71 (3.84)	4.84 (3.57)	4.43 (3.76)	4.31 (3.65)	5.16 (3.79)	4.81 (3.57)
- Borderline n (%)		120 (15%)	40 (13%)	80 (15%)	48 (13%)	72 (16%)	48 (10%)	40 (21%)	32 (18%)
- Moderate/severe n (%)		55 (7%)	16 (5%)	39 (7%)	26 (7%)	29 (6%)	32 (7%)	14 (7%)	9 (5%)
MSPSS – median (IQR)									
Total support	820	1.50 (1.08-2.25)	1.58 (1.17-2.33)	1.50 (1-2.08)	1.58 (1.08-2.25)	1.42 (1.08-2.17)	1.50 (1.08-2.25)	1.58 (1-2.25)	1.50 (1.17-2.08)
Support - friends	827	7 (4-11)	7 (4-12)	6 (4-10)	7 (4-11)	6 (4-10)	7 (4-10)	7 (4-12)	7 (4-10)
Support - family	827	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	4 (4-7)
Support – significant others	823	4 (4-8)	5 (4-9)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-9)	4 (4-7)
BIPS – median (IQR)	830								
Consequences		7 (4-8)	7 (5-8)	7 (4-8)	7 (5-8)	6 (4-8)	6 (4-8)	7 (5-8)	7 (6-9)
Personal control		6 (4-8)	6 (5-8)	5 (3-8)	6 (4-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Treatment control		10 (9-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (9-10)	10 (8-10)
Identity		5 (3-7)	6 (3-8)	5 (3-7)	6 (4-7)	5 (2-7)	5 (3-7)	6 (3-8)	6 (4-8)
Coherence		8 (7-10)	9 (7-0)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	9 (7-10)
Emotional representation		6 (4-8)	5 (3-7)	7 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (3-8)
Concern		6 (3-8)	5 (3-7)	7 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Satisfaction with care – n (%)	820								
Excellent/good		777 (95%)	284 (95%)	493 (95%)	358 (96%)	419 (94%)	433 (95%)	173 (91%)	171 (99%)

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Fair/poor/very poor		43 (5%)	16 (5%)	27 (5%)	15 (4%)	28 (6%)	23 (5%)	18 (9%)	2 (1%)

BIPS: Brief Illness Perception Scale; EQ-5D: Euroqol 5-Dimension; HADS: Hospital Anxiety and Depression Scale; IRQ: interquartile range; MSPSS: Multi-dimensional Scale of Perceived Social Support; PedsQL: Pediatric Quality of Life Questionnaire;SD: standard deviation

[1]Borderline = 8-10, moderate/severe = >11 [49]

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DISCUSSION

The BRIGHTLIGHT cohort is the first national, prospectively recruited cohort of teenagers and young adults with cancer. We are able to examine in detail the complexity associated with place of care, experience and outcome. This is made possible through the use of linked data from multiple sources so unlike other cohorts which rely solely on patient-reported outcomes [34, 54] or clinical data [32], a more comprehensive evaluation can be derived. Using national mandatory NHS datasets we have been able to calculate a more robust measure of time spent in specialist TYA care. Other data sources, such as secondary analysis of the National Cancer Patient Experience data is based on TYA PTC code at the time of participation [55], as such this reflects a single point in time and does not reflect experiences and outcomes for those who have exposure to both specialist and non-specialist care. Measuring exposure to a TYA PTC through analysis of HES data has enabled a more objective exposure variable to be developed. Similarly, defining severity of cancer through prognosis for survival alone does not reflect the symptom/treatment burden of disease and the impact this has on quality of life during treatment and recovery. Systematically defining prognosis alongside symptom and treatment burden, provides a more nuanced measure and is a better reflection of the severity of illness.

Selecting the study design to evaluate TYA cancer services across England was challenging as services were already in place and, in some regions of the country, long-established. There was also wide variation in implementing the NICE Guidance [1] according to local need and pre-existing resources, resulting in services at PTCs not being identical. The decision to establish a cohort was made on the basis that it is suited for investigating rare exposures, allows examination of multiple outcomes for the defined exposure (to specialist care), and would enable us to gather data regarding sequence of events, with the potential to assess causality. The main limitation of the cohort is we only recruited a fifth of the population who were eligible to participate. Variation in diagnosis and severity between those in the cohort receiving different level of PTC care reduces the potential to assess causality.

Cohort studies are acknowledged to be challenging to establish and maintain, especially in rare conditions due to the requirement for large numbers of subjects, potential for selection bias and the challenges associated with subject retention [56-59]. We anticipated that participation might favour those who were less unwell or had a better prognosis. The inclusion of significant numbers with tumours associated with poorer prognosis such as bone tumours and the inferior survival of the cohort go against this. One of the aims of the BRIGHTLIGHT was to evaluate socioeconomic variation in access to specialist care. A comparison of IMD quintile between those who were and were not recruited who have enabled us to assess whether there was bias in recruitment according to difference socioeconomic groups; however, these data were not available but warrant exploration in the future. Our experience of recruitment points to the value of maintaining accurate screening logs and seeking mechanisms to complement the intelligence from local teams about change of status of participants such as death or change of address.

Our experience highlights the value of patient and public participation in research. We have described earlier in the paper the involvement young people had from study inception to

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dissemination. In total more than 1,200 young people have been involved in BRIGHTLIGHT as part of the research process almost the same number as those recruited. We believe this has positively influenced the rates of participation, ways in which young people were approached and methods of data collection, and doubled the retention rate at Wave 3 [7].

This population is known to have lower involvement in clinical trials in comparison to children and older adults [22, 60], yet there have been no targeted interventions developed to improve recruitment [61]. We have reported that to optimise recruitment to clinical trials, what we have identified as 'the 5'A's' need to be addressed, namely availability, accessibility, awareness, appropriateness, and acceptability [60]. We have identified factors that young people feel are acceptable for accessing research [8] and for continuing their involvement in a study [7]. We have also identified that the networked structures for facilitating recruitment into cancer research in England may not be optimal for the recruitment of young people [41]. The impact of not having an optimal research network was made apparent through BRIGHTLIGHT, as it was the first national study in this population. Ways to overcome this challenge are currently being explored by the NIHR.

FUTURE PLANS

The BRIGHTLIGHT cohort was originally designed to evaluate short-term outcomes, from early after diagnosis to three years after diagnosis, over five time points. Data collection for wave 5 ended in February 2018, with results for the four key objectives anticipated to be available by the end of 2018. As noted earlier, the study has generated a large quantity of data and with the recent completion of a James Lind Alliance Priority Setting Partnership exercise for TYA exercise (http://www.ncri.org.uk/ncri-blog/top-10-research-priorities-for-teenage-and-young-adult-cancer-identified/), there is the opportunity to address some of the unanswered questions with the BRIGHTLIGHT cohort. This opportunity has already been realised to contribute evidence to improvements in early diagnosis [19]. In line with NIHR guidance, patient-reported outcome data from the cohort will be made available to external researchers on acceptance of the final report in the NIHR Journal Library. Details of how to apply will be made available on the website (www.brightlightstudy.com).

The philosophy of specialist TYA cancer care is to provide optimal cancer treatment alongside the developmentally-sensitive care that enables young people to achieve their life goals (e.g. education, employment, relationships) during treatment and beyond. BRIGHTLIGHT will evaluate this in the short-term but longer-term follow-up may be valuable to explore whether the model of care delivery influences these outcomes later in life. We are now planning a 10-year follow-up study to assess the long-term impacts. We also acknowledge that similar to other studies quantifying care using NHS data [55, 62], the measure of specialist care may lack discrimination, not least because it assumes that all TYA PTCs and other places of care are equal. Additional to the cohort, a case study was conducted to understand the culture of TYA cancer care [3]. There is the potential to synthesise the qualitative findings from the case study with the quantitative data from the cohort to develop a more detailed and sensitive metric to define specialist TYA cancer care. Ultimately, the data generated by the cohort and BRIGHTLIGHT will provide new information on cancer in young people and determine if access to a PTC adds value. The relationships

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between specialist care and outcomes have previously been unclear. Findings will inform intervention and policy efforts to improve outcomes for young people with cancer.

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RMT, LAF, JB, DS, SM, RF, LH, FG, RR, JSW were involved in developing the protocol. RMT coordinated the running of the study and was responsible for data acquisition. JB, JGA, RMT, LAF, SM, RF, MM, DS, JSW contributed to the analysis. RMT, LAF, JB and JSW drafted the manuscript. All authors critically revised and approved the final manuscript.

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FOLLOWING REVIEW

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Competing interests:
None declared.

Ethics Approval:
The study was approved by the Health Research Authority Confidentiality Advisory Group (reference ECC 8-05(d)/2011) and London Bloomsbury NHS Research Ethics Committee (reference LO/11/1718).

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Data sharing statement:
Further details of the BRIGHTLIGHT programme of work is available through the study website (www.brightlightstudy.com). Data that are not held under licence with Public Health England or NHS Digital will be available from late 2018 when the primary analysis is complete. We welcome collaboration, for general data sharing enquiries please contact RMT (rtaylor13@nhs.net).

FOLLOWING REVIEW

Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures

i. Open to most Trusts agreeing to participate (n=77); posters to advertise BRIGHTLIGHT distributed to all Trusts
ii. Information to all newly diagnosed young people distributed in CLIC Sargent information packs; top recruiters reported in the TYAC weekly bulletin (the professional organisation in the UK supporting healthcare professionals with adolescents and young adults with cancer)
iii. Healthcare professional information leaflets sent to all Trusts (hard copy and electronic for local distribution)
iv. Director/Assistant Directors of the National Cancer Research Network emailed all the Cancer Network Managers directing them to make recruitment to BRIGHTLIGHT a priority; approved amendment to allow consent to be taken the same time a giving the information sheet
v. Review of screening logs and site specific feedback presentations sent to each Principal Treatment Centre (PTC)
vi. Open to recruitment in all 13 PTCs
vii. Approval to use social media to recruit young people; open in all 109 Trusts agreeing to open to recruitment
viii. Attendance at a Teenage Cancer Trust Lead Nurse event to highlight recruitment issues and gain support
ix. Emails sent by universities (communication teams or student unions) to current students with a link to the website to capture young people continuing with education after diagnosis; training for Youth Support Coordinators to be able to recruit young people
x. Attend a CLIC Sargent Social Worker event to promote the study and gain support to take a recruitment role
xi. Information on the BRIGHTLIGHT website in video format
xii. Recruitment method based on the National Cancer Patient Experience Survey implemented

Figure 2: A summary of participation at each wave of data collection

* Drop outs between waves due to death, permanent opt-out or wave opt out. Wave opt-outs prior to being issued were not permanent opt-outs; participants could opt-out of a single wave but participate in subsequent waves; these cases were not removed from the cohort permanently

Figure 3: Comparison of survival between participants in the Cohort and non-participants[1]

Estimated cumulative survival probabilities by year from diagnosis (95% CI)		
	Non-participants	BRIGHTLIGHT cohort
1 year	0.98 (0.97, 0.98)	0.98 (0.97, 0.99)
2 years	0.95 (0.94, 0.96)	0.92 (0.91, 0.94)
3 years	0.93 (0.92, 0.94)	0.89 (0.87, 0.91)
4 years	0.92 (0.91, 0.93)	0.88 (0.85, 0.90)

CI: confidence intervals
Log rank test P value <0.0001
[1]Non-participants were young people diagnosed in the same time frame as the BRIGHTLIGHT cohort identified by the National Cancer Registration and Analysis Service (NCRAS), who were not part of BRIGHTLIGHT

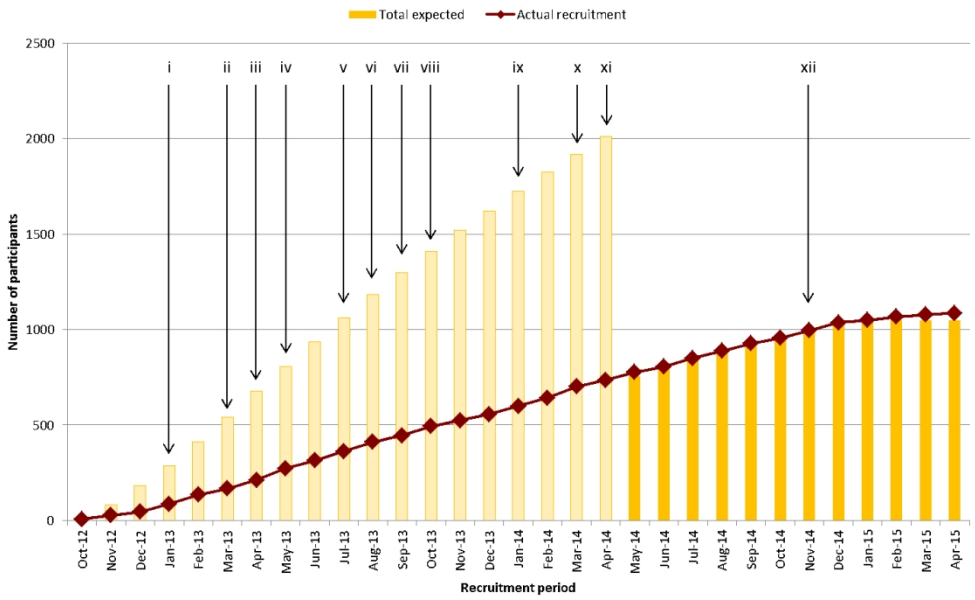


Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures

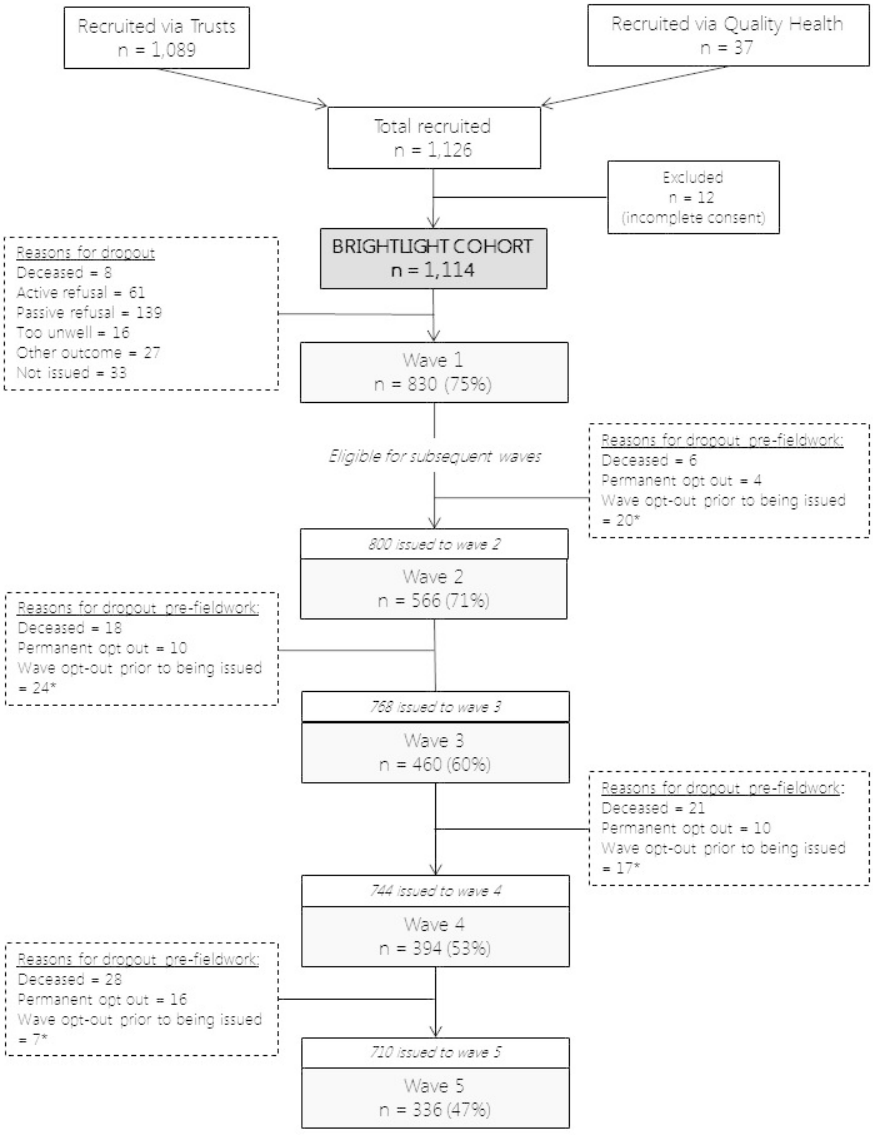


Figure 2: A summary of participation at each wave of data collection

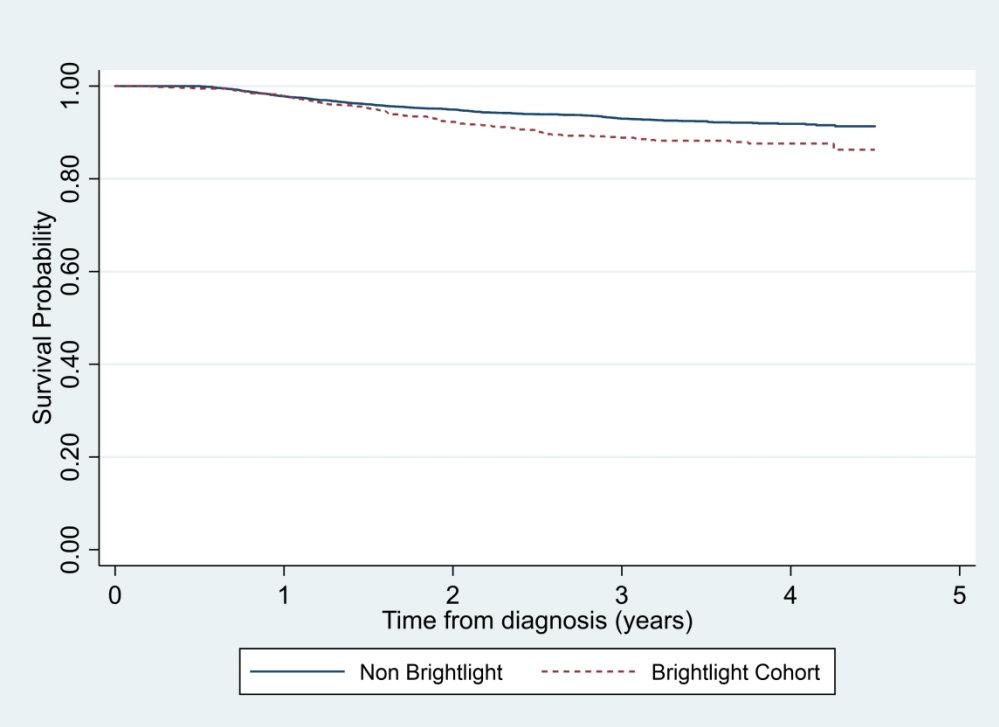


Figure 3: Comparison of survival between participants in the Cohort and non-participants

BRIGHTLIGHT Cohort profile – supplementary file 1

Supplementary File 1 Detailed results of actions implemented to improve recruitment to the cohort

Table A: Possible challenges reported by healthcare professionals before recruitment began and strategies identified to overcome them

	Challenges	**Strategies proposed to overcome challenges**
Identifying young people	Missing eligible young people if transferred to regional specialist centres Recruiting across a range of hospital sites Recruiting across multiple tumour types Engaging consultants: one concern was they would not think the older TYAs were eligible, a perception being that it was a 'teenager' study	Use the TYA MDT meetings to identify young people Co-ordination by a key person such as the Lead Nurse, cancer network head, or MDT lead to ensure details of eligible TYAs are passed to the recruiters Collaborative working with other centres to ensure all young people are approached, but not on multiple times
Approaching/consenting young people	Concerns about 'getting past' protective and upset parents Timing of consent, particularly if the patient is undergoing chemotherapy and was likely to be feeling very unwell Lack of experience in working with 'children' Being seen or felt to 'pressurise' potentially 'vulnerable and fragile' young people to take part Getting treating consultant approval to approach young people	Encouraging the initial approach to be a conversation, and not be immediately about persuading young people to take part Work with paediatric nurses to help with recruiting younger TYA Undertake paediatric consent training Wait for a sufficient length of time after diagnosis – maybe two months – before introducing the study, to allow the young person to become accustomed to the emotional and practical impact of the diagnosis

TYA: Teenage and young adult; MDT: multi-disciplinary team

BRIGHTLIGHT Cohort profile – supplementary file 1

Table B: Suggestions from healthcare professionals for keeping young people engaged throughout the study

Suggestion to keep young people engaged	Action for implementation by BRIGHTLIGHT
Get the consent process absolutely right: clear, accurate information about the survey, as buy-in from young people will increase the chances they will continue to participate	Information developed with young people, site initiation with recruiters to ensure they knew about the study and could relay information to young people in the best way
Provide TYA-friendly formats: e.g., ensure the survey could be completed on an iPad or iPhone as well as on a home computer	The survey was administered face-to-face at the first time point; subsequently it could be completed online on any platform
Use the internet: communicate via social networks like Facebook and Twitter	An open Facebook account was prohibited by the sponsor Trust but a Twitter account was opened
Ensure language used is aimed at empowering young people	All information was reviewed by the YAP[1] and had a reading ease of >70%
Consider incentives: e.g., a medal-based reward system – for each year young people remain in the study they move up the medals from Bronze (Year 1) to Silver (Year 2) and Gold (Year 3) and get a correspondingly increasingly valuable reward each time.	The YAP suggested a reward system using wrist bands with a different colour for each wave of participation
Inform participating young people on why the study matters and why their continuing involvement is important	A website was developed to keep young people updated about the programme www.brightlightstudy.com
Maintain contact throughout	Newsletters
Disseminate progress and results so they can see the wider scale and impact of the survey, that is making a difference	Content of newsletters related to results as far as was possible
Keep parents on board perhaps with targeted communications	Newsletters sent to all the email addresses provided
Distribute posters and flyers to treatment centres	Posters and flyers provided

YAP: Young Advisory Panel; TYA: teenage and young adult

[1]YAP are the BRIGHTLIGHT patient user group

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C: Suggestions for how the BRIGHTLIGHT Team might facilitate recruitment and actions taken to address these

Suggested change	Action by the BRIGHTLIGHT Team
1. Study information for health professionals	An information booklet was developed giving a brief summary of the study. This was sent electronically and as hard copies to all participating Trusts. Regular newsletters were developed and circulated online and as hard copies. Recruitment figures were circulated in a weekly Bulletin by TYAC to their members and were also Tweeted by the BRIGHTLIGHT team (@bR1GhTLiGhT)
2. Make the participant information sheets as short as possible	A summary booklet had been produced by Ipsos MORI[1] to send as a reminder about the study by their interviewers. An ethics amendment was made in July 2013 to allow this to be used in conjunction with the lengthy information sheet at the time of consent. Video versions of the information sheet were made available on the website (www. http://www.brightlightstudy.com/user-involvement/)
3. Investigate any variation in recruitment rates between sites	Screening logs were requested and analysed to identify reasons for suboptimal recruitment, which was fed back to each Trust with guidance on how to overcome recruitment issues.
4. Reduced interval between giving information and getting consent[2]	An amendment was approved by the Ethics Committee to allow consent to be taken within the same 24-hour period as information was given.
5. Provide BRIGHTLIGHT advertising materials	Posters, flyers and postcards had been available since the beginning of the study. These were distributed not only by the BRIGHTLIGHT Team but also by CLIC Sargent and Teenage Cancer Trust.
6. Keep sending the NWCIS notification[3]	There was a temporary pause in the CWT data being sent due to organisational change of NWCIS to Public Health England.
7. Extend the window of recruitment for wave 1	This was relaxed at the end of 2012 so young people could be recruited at any time in the first four months after diagnosis. We were unable to extend recruitment beyond this period because we wanted data to be collected within a specific time window. Young people were not able to enter the study at later time points because subsequent questions were informed by responses in the first survey.

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C. *cont.*

Suggested change	Action by the BRIGHTLIGHT Team
8. Reduce the number of times young people need to participate (total study participation involved 5 time points in 3 years)	The sample size calculation was based on participation at three time points (as specified in the protocol) because we were aware young people might opt in and out of participation depending on their current life commitments. We developed top tips for recruiting Trusts, including information about participation. The top tips were prominent on the website, were sent as an information leaflet, and included in the newsletter.
9. Enable information sheets to be posted to young people	An ethics amendment was approved to enable information sheets and consent forms to be posted and/or returned through the mail.
10. Make presentations at local network and Trust meetings	Members of the BRIGHTLIGHT team presented recruitment updates at every available national meeting. Trusts were also informed that the team would come to any local meetings on request. Site specific slides to present at MDTs were provided to all PTCs.
11. First survey to be online or telephone rather than face-2-face	This request could not be accommodated. A single mode of administration had been developed for the first survey.[4]

CWT: Cancer Wait Time database; MDT: multi-disciplinary team; NWCIS: North West Cancer Intelligence Service (after the move to Public Health England became known as the North West Knowledge Intelligence Team). PTC: Principal Treatment Centre; TYAC: Teenagers and Young Adults with Cancer (the organisation representing healthcare professionals working in this area).

[1] Ipsos MORI were the commercial company administering the BRIGHTLIGHT Survey; [2] Ethics guidance in the United Kingdom recommends a minimum of 24 hour between providing information and gaining consent to give participants time to process information; [3] NWCIS sent a monthly email to a dedicated person in each recruiting trust with a list of potentially eligible patients identified through the Cancer Waits dataset as newly starting treatment; [4]Subsequent waves had a choice of online or telephone interviewer administered survey; the online option has only been selected by a minority of young people

BRIGHTLIGHT Cohort profile – supplemental file 2

Supplemental file 2: Method for calculating the TYA Cancer Specialism Scale (TYA CSS) to assign level of care

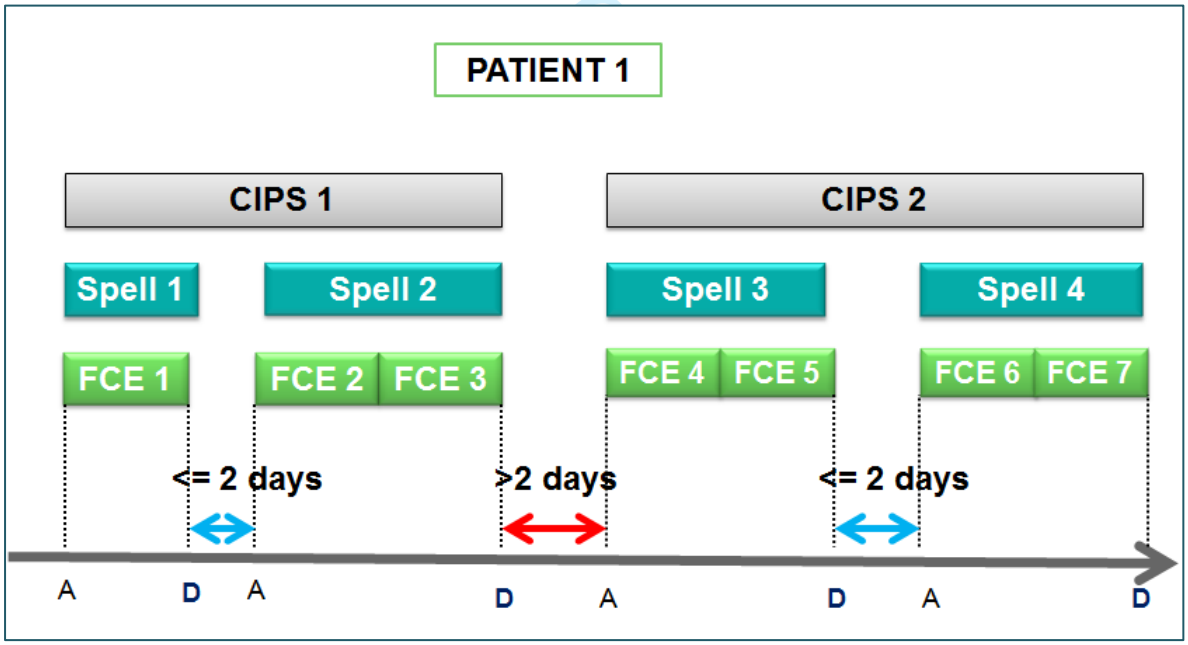
The TYA CSS is derived from admitted patient care data using linked Hospital Episode Statistic (HES) data. HES data from 2011/12 to 2016/17 were obtained from NHS Digital and linked to patients from the BRIGHTLIGHT cohort using the following identifiers: NHS Number, sex and postcode. The method for calculating the TYA CSS is adapted from an approach first proposed by Birch in 2013[1].

Hospital activity within HES is recorded in three ways (Figure 1):

1. Finished consultant episodes (FCEs)
2. Spells (sequential hospital encounters with different consultants)
3. Continuous inpatient spells (CIPS: hospital admissions for the same patient receiving care from different consultants and different providers/trust within two days after discharge)

FCE is the standard measurement unit for hospital activity and considered to provide more accurate estimates of consultant workload and hospital resources[2]. FCE was used for the basis of analysis and derivation of the TYA CSS to ensure we used all available data on consultant care at the deepest level of granularity available.

Figure 1: Different classifications of hospital admission for an example patient based on HES



Abbreviation: FCEs -finished consultant episodes, CIPs -continuous inpatient spells, A-admission, D- discharge.
Source: Analysing Patient-Level Data Using Hospital Episode Statistics (HES), University of York.

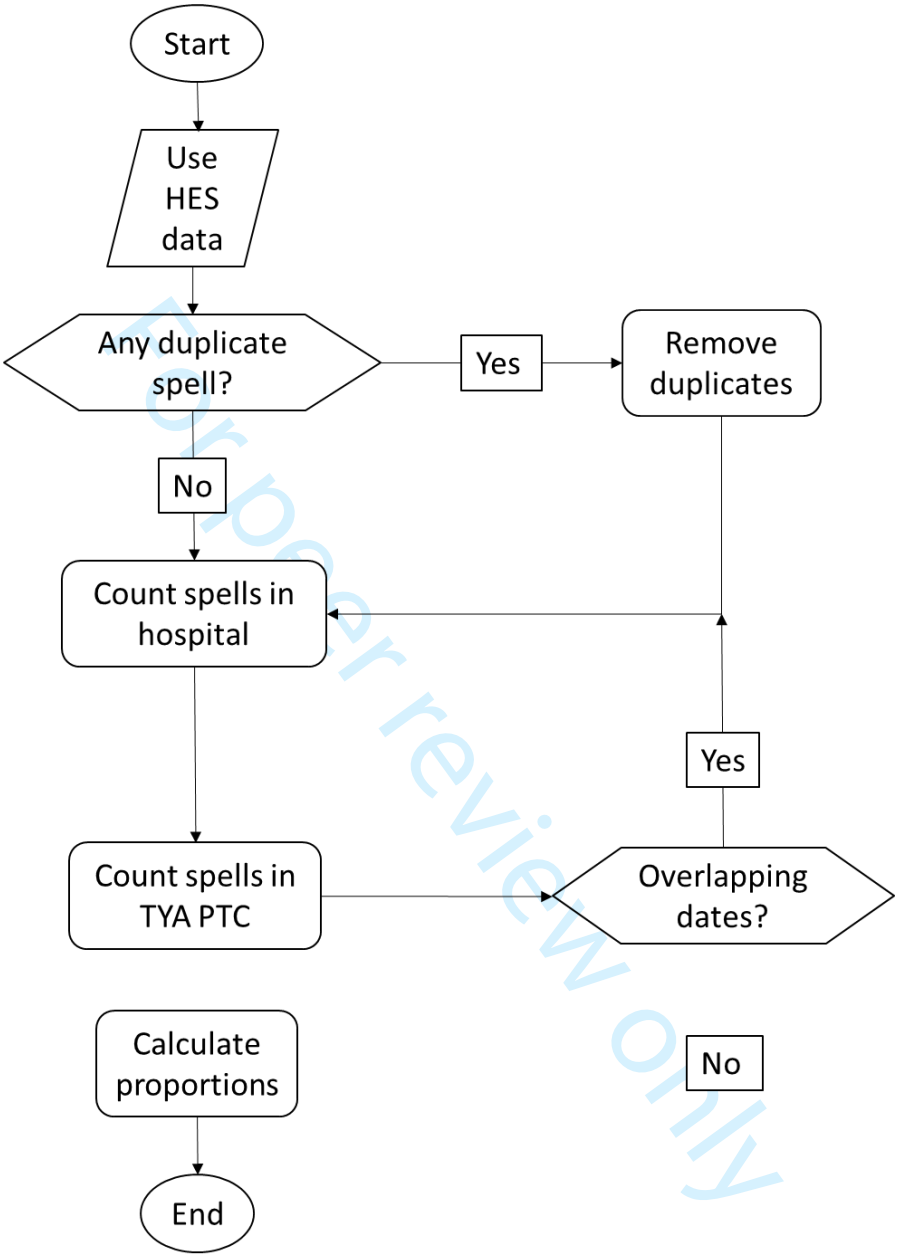
[1] Birch RJ. Teenage and young adult cancer in England – the patient journey and experience. The University of Leeds, PhD Thesis 2013

[2] Hargreaves DS, Viner RM. Adolescent inpatient activity 1999–2010: analysis of English Hospital Episode Statistics data. Archives of disease in childhood 2014; 99: 830-833

BRIGHTLIGHT Cohort profile – supplemental file 2

The development of the TYA CSS is summarised in Figure 2.

Figure 2: Summary of the process for calculating the TYA CSS



Data cleaning

HES data were cleaned to remove duplicates and to clarify some of the diagnostic coding. Reference was made to the HES admitted patient care data dictionary[3] to guide the data cleaning process in order to ensure accuracy and consistency in the recording and analysis of the HES records.

Duplicates were removed to ensure there were not several copies of the same admission being recorded for the same patient. These were identified by ascertaining whether more

[3] HSCIC. HES data dictionary. HEALTH AND SOCIAL CARE INFORMATION CENTRE 2016, 20 January 2016; Available from: http://www.hscic.gov.uk/hesdatadictionary

than one admission began on the same date for a single patient and then cross checking this against admission reasons, procedure codes and treating physician code. Examples of fields which would be indicative of duplicate admission records include multiple HES_IDs, episode start date, episode end date, admission date and discharge date.

Location of specialist care centres

The aim of the study is to evaluate the value of specialist cancer services. 'Specialist' was originally defined in the *Improving Outcomes Guidance (IOG)*[4] as 13 principal treatment centres (PTCs) across England. To account for the age range of the BRIGHTLIGHT cohort starting at 13 years, PTCs also included children's PTCs where the age of admission for the TYA PTC did not include younger adolescents (Table 1). The hospital codes for the look up tables were taken from NHS Digital[5].

Calculation of the scale

The level of specialist care received was calculated from the time of diagnosis (taken from the date recorded in the National Cancer Registration and Analysis Service dataset)

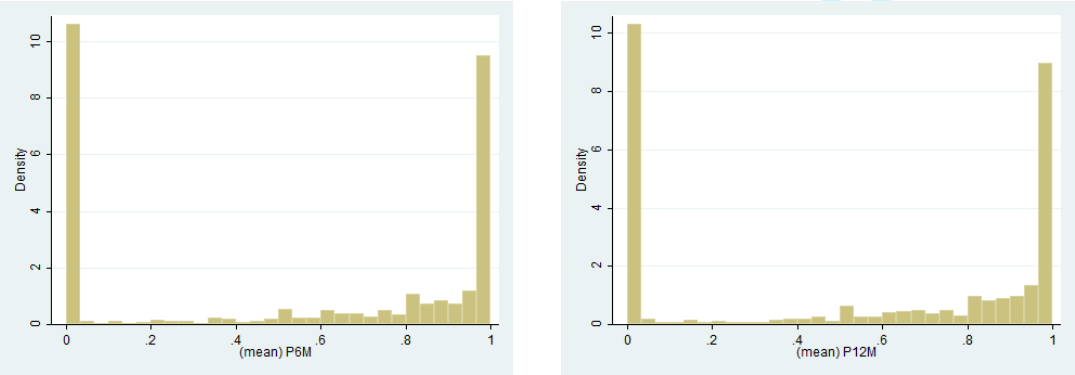
1. Six months after diagnosis: Spells in TYA PTC from diagnosis at 6 months/Total spells from diagnosis at 6 months
2. 12 months after diagnosis: Spells in TYA PTC from diagnosis at 12 months/Total spells from diagnosis at 12 months

For every individual, HES data were used to calculate the number of inpatient and day case bed days spent in a specialist centre (A), as well as the number of total bed days across all secondary care services (B) within the first 6 and 12 months after diagnosis. The proportion of time spent in a specialist centre was then derived as (A)/(B).

Defining the levels of care

Inpatient HES data were successfully linked to 1,074 out of 1,114 young people recruited to BRIGHTLIGHT. The distribution of the proportion of care by 6 months and 12 months after diagnosis suggested there were three natural groups occurring within the data (Figure 3).

Figure 3: Distribution of the proportion of care receive in a TYA PTC



[4] National Institute for Health and Care Excellence. Guidance on cancer services: improving outcomes in children and young people with cancer. NICE, London 2005https://www.nice.org.uk/guidance/csg7/resources/improving-outcomes-in-children-and-young-people-with-cancer-update-773378893 [Accessed 30/08/18]

[5] https://digital.nhs.uk/services/organisation-data-service

BRIGHTLIGHT Cohort profile – supplemental file 2

Table 1: List of principal treatment centres in England (2012-2014) for young people aged 13-24 years

Principal Treatment Centre	**Hospital**
Cambridge University Hospitals NHS Foundation Trust	Addenbrookes Hospital (aged 14-24)
The Christie NHS Trust	Christie Hospital (aged 16-24)
Manchester University Hospitals NHS Foundation Trust	Royal Manchester Children's Hospital (aged 13-15)
Clatterbridge Centre for Oncology NHS Foundation Trust	Clatterbridge Centre (aged 16-24)
Alder Hey Children's NHS Foundation Trust	Alder Hey Children's Hospital (aged 13-19)
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Royal Liverpool Hospital
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Broadgreen Hospital
Leeds Teaching Hospitals NHS Trust	Leeds General Infirmary (aged 13-16)
Leeds Teaching Hospitals NHS Trust	St James's University Hospital (aged 17-24)
Nottingham University Hospitals NHS Trust	City Campus (aged 18-24)
Nottingham University Hospitals NHS Trust	Queens Medical centre (aged 13-18)
Sheffield Teaching Hospitals NHS Foundation Trust	Weston Park Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Royal Hallamshire Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Sheffield Children's Hospital (aged 13-16)
Southampton University Hospitals NHS Trust	Southampton General Hospital (aged 16-24)
Southampton University Hospitals NHS Trust	Southampton Children's Hospital (aged 13-15)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Northern Centre for Cancer Care (aged 19-24)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Royal Victoria Infirmary (aged 13-18)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Sutton (aged 13-24)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Fulham (aged 17-24)
University College London Hospitals NHS Foundation Trust	University College Hospital (aged 13-24)
University College London Hospitals NHS Foundation Trust	Cancer Centre (aged 13-24)
University Hospital Birmingham NHS Foundation Trust	Queen Elizabeth Hospital (aged 16-24)
Birmingham Children's Hospital NHS Trust	Birmingham Children's Hospital (aged 13-18)
University Hospital Bristol NHS Foundation Trust	Bristol Haematology & Oncology Centre (aged 17-24)
University Hospital Bristol NHS Foundation Trust	Royal Hospital for Children (aged 11-16)
University Hospital Bristol NHS Foundation Trust	Bristol Royal Infirmary
University Hospital Bristol NHS Foundation Trust	St Michael's Hospital
University Hospitals of Leicester NHS Trust	Leicester Royal Infirmary (aged 13-24)
Oxford University Hospital NHS Trust	Churchill Hospital (aged 18-24)
Oxford University Hospital NHS Trust	John Radcliffe Children's Hospital (aged 13-18)

BRIGHTLIGHT Cohort profile – supplemental file 2

Supplementary File 2: Development of the BRIGHTLIGHT Severity of Illness Index (BRIGHTLIGHT SIX)

Rationale for developing a bespoke severity index

Within the BRIGHTLIGHT cohort, place of care was not randomly assigned but instead determined by local pathways of care, key influences including the type of cancer, age, proximity to principal treatment centres. As a consequence, differences exist between those who have all/some of their treatment in the teenage and young adult (TYA) Principal Treatment Centre (PTC) and those who have had no care in a TYA PTC. This fundamental difference between the populations of patients who receive no, some or all TYA PTC care was thought likely to be a major confounder in the interpretation of any observed differences in patient experience and outcome between these groups. The differences may not be reflected accurately if cases were grouped solely by, say, tumour type or disease stage due to the considerable variation between tumour types and between similar tumours of different stages in the intensity of treatment received and the likelihood of survival. To interpret the significance of any observed differences in our primary or secondary outcome measures across the populations with no, some or all TYA PTC care, we needed a measure that would allow comparison across patients with different tumours, but capable of discriminating between patient populations. Our primary outcome was quality of life (QOL) and a powerful determinant of QOL is 'the burden of cancer' patients had at diagnosis[1]. We wished to consistently and systematically describe the burden of cancer to assist analysis. The severity of illness index therefore needed to reflect prognosis, disease morbidity (symptoms, physical impact) and treatment morbidity (determined by treatment duration, intensity and anticipated late morbidity burden).

The BRIGHTLIGHT Severity of illness index (SIX)

Constructing the index

All cancer types were compared by symptom burden, treatment burden and prognosis using germ cell tumours as a reference: Stage 1 – very likely to survive, treatment either surgery alone or surgery plus a limited burden of chemotherapy, few if any anticipated late effects of treatment; Stage 2-3 – ~90% survival, many have intensive or multimodality treatment or larger operations, some late toxicity burden; Stage 4 – 50% survival and intensive treatment. Stage 4 we classed as 'most severe' and used this as a reference point to compare odds of survival and treatment burden for other cancers.

Germ cell tumours were chosen as a reference because they are relatively common in the TYA age group, have a range of prognoses from excellent to poor, and treatments have a range of morbidity from surgery alone through to very intensive chemotherapy with both acute and long-term sequelae.

[1] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

BRIGHTLIGHT Cohort profile – supplemental file 2

Three clinicians and two BRIGHTLIGHT researchers reviewed all cancer types to consider allocation to one of three severity levels. Survival estimates were based on examination of current or recently completed trial protocols where available and using a recently published comprehensive TYA-specific reference textbook[2]. We evaluated treatment burden using duration and expected toxicity from multiple sources, including clinical experience, trial protocols, a current TYA oncology text book and international guidelines (such as the National Comprehensive Cancer Network). In addition, other potentially comparable clinical severity scales were sought from the literature to determine comparability or utility in this context.

Content validity of the index

Once a preliminary scale had been constructed, its content was tested by expert review. At least two additional clinicians with specialist clinical expertise were approached to review each tumour type. The reviewers were sent a short document outlining the purpose of the scale and its development to that point as well as the scale itself. They were interviewed either face-to-face or by telephone by a senior clinician and BRIGHTLIGHT researcher (JSW) and asked to respond to two questions:

1. *Within the row(s) of the cancer types in which you have particular expertise (e.g. central nervous system tumours), do you agree with the allocation of grades of severity?*
2. *Looking at other tumour types, by comparison with other rows, do you agree with the allocation of grades of severity?*

Interviews were recorded and field notes taken. The scale was adjusted in response to expert comments to produce a final version (main paper, Table 2).

Applying the BRIGHTLIGHT SIX

BRIGHTLIGHT researchers (RMT, LAF, DS) independently allocated a severity level to each patient, conducting these assessments blind to responses to the survey, including QOL results. Comparisons between the three scores were made and, where there were differences, adjudication through a fourth researcher (JW) determined whether this was an error or due to ambiguity in the Index.

Other measures of severity

We found only one other example in which investigators had categorised TYA by cancer severity. Husson et al[1] used expected 5-year survival to divide patients into three groups, those with expected survival of greater than 80%, 50-80% and less than 50%.[3] Using the same source data[4], we also allocated each patient from the BRIGHTLIGHT cohort a second severity level based on 5-year survival.

We compared this method (Five year survival index, FYX) with BRIGHTLIGHT SIX. As anticipated, those judged to have the most severe cancer by BRIGHTLIGHT SIX are

[2] Bleyer, Barr, Ries, Whelan, Ferrari eds. Cancer in Adolescents and Young Adults. Springer International Publishing, Switzerland 2017

[3] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

[4] Bleyer, A. (2011). "Latest Estimates of Survival Rates of the 24 Most Common Cancers in Adolescent and Young Adult Americans." J Adolesc Young Adult Oncol 1(1): 37-42.

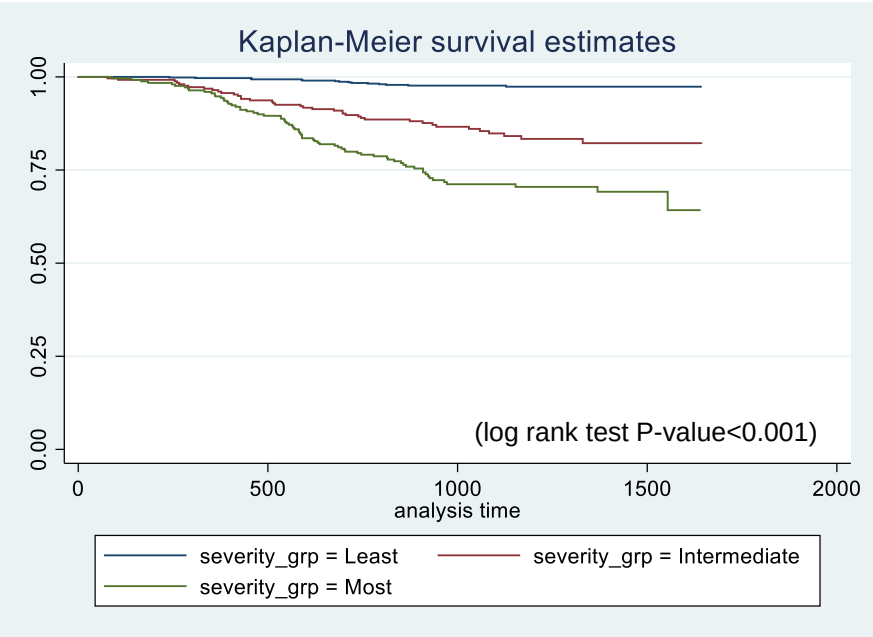
distributed across the three survival categories though weighted towards the two lower survival groups. Similarly, most but not all of those with the least severe cancer by BRIGHTLIGHT SIX had the best expected survival. Those with intermediate severity cancer are spread across the three FYX groups (Table 1).

Table 1: Comparison between the Five year survival Index (FYX) and BRIGHTLIGHT Severity of Illness Index (SIX)

	SIX level		
FYX	Least	Intermediate	Most
<50%	1	100	71
50-80%	56	98	171
>80%	546	56	7

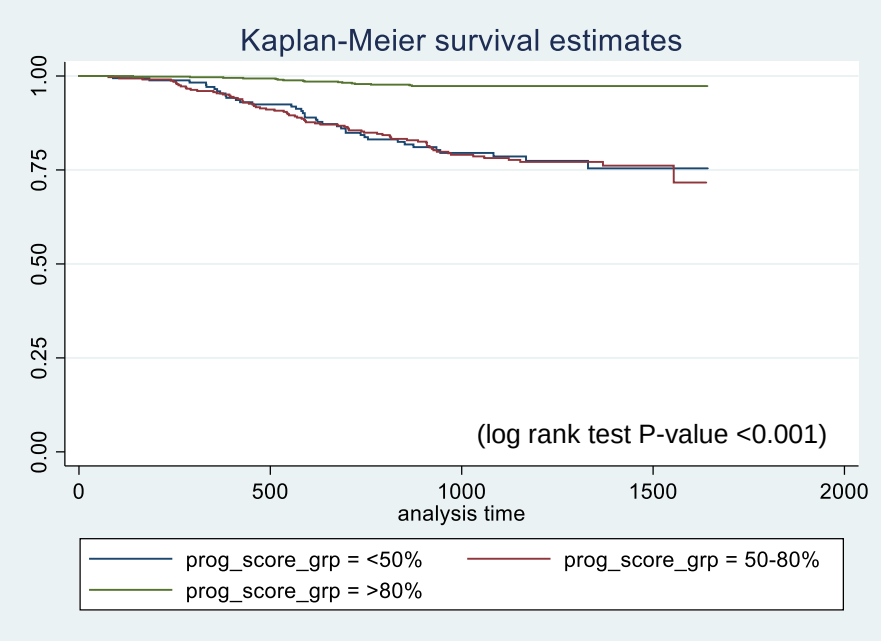
We then analysed survival of the BRIGHTLIGHT cohort using the two indices. Figure 1 demonstrated a clear discrimination in survival by BRIGHTLIGHT SIX, consistent with anticipated survival being an important but not sole component of the index. The survival of the BRIGHTLIGHT cohort was then examined by allocated FYX category (Figure 2). FYX failed to distinguish three groups with distinct survival as that of those allocated to the two lower categories was superimposed.

Figure 1: Survival by BRIGHTLIGHT Severity of Illness Index



BRIGHTLIGHT Cohort profile – supplemental file 2

Figure 2: Survival of BRIGHTLIGHT cohort against allocated FYX group



STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-9*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	Not applicable
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	Not applicable – only reporting baseline

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	characteristics
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 2
		(b) Give reasons for non-participation at each stage	Figure 2
		(c) Consider use of a flow diagram	Figure 2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	Tables 3-5
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable, presenting wave 1 data only
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable – wave 1 descriptive data only
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Descriptive data only presented
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Description of the BRIGHTLIGHT Cohort: the evaluation of teenagers and young adult cancer services in England

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Description of the BRIGHTLIGHT Cohort: the evaluation of teenagers and young adult cancer services in England

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ABSTRACT

Objective: International recognition of the unique needs of young people with cancer is growing. Many countries have developed specialist age-appropriate cancer services believing them to be of value. In England, 13 specialist Principal Treatment Centres (PTC) deliver cancer care to young people. Despite this expansion of specialist care, systematic investigation of associated outcomes and costs has to date, been lacking. The aim of this paper is to describe recruitment and baseline characteristics of the BRIGHTLIGHT cohort, and the development of the bespoke measures of levels of care and disease severity, which will inform the evaluation of cancer services in England.

Design: Prospective, longitudinal, observational study.

Setting: Ninety-seven NHS hospitals in England.

Participants: A total of 1,114 participants were recruited diagnosed between July 2012 and December 2014: 55% (n=618) male, mean age was 20.1 years (SD=3.3), most (86%) were white and most common diagnoses were lymphoma (31%), germ cell tumour (19%) and leukaemia (13%).

Results: At diagnosis, median quality of life score was significantly lower than a published control threshold (69.7 points); 40% had borderline-severe anxiety, and 21% had borderline-severe depression. There was minimal variation in other patient-reported outcomes according to age, diagnosis or severity of illness. Survival was significantly worse in the Cohort than for young people diagnosed during the same period who were not recruited (cumulative survival probability 4 years after diagnosis: 88% vs. 92%).

Conclusions: Data collection was completed in March 2018. Longitudinal comparisons will determine outcomes and costs associated with access/exposure to PTCs. Findings will inform international intervention and policy initiatives to improve outcomes for young people with cancer.

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Strengths & limitations of this study

5 bullet points

- This is the largest ever prospective cohort of young people with cancer, examining not only cancer outcomes but also the social and educational impact of a cancer diagnosis.
- The socio-demographic characteristics of the cohort are broadly similar to the contemporary total teenage and young adult cancer population thus increasing the generalisability of results.
- Data has been collected from multiple sources, results therefore reflect the perspective of the patient, plus clinical care and data on health service use.
- Study results will provide new information on cancer in young people and determines if access to a Principal Treatment Centre adds value; the relationships between specialist care and outcomes have previously been unclear. Findings will contribute to intervention and policy efforts to improve outcomes and patient experience for young people with cancer
- The cohort comprises 20% of young people diagnosed with cancer during the time period. A decrease from original target sample size (n=2,012) consequent of recruitment difficulties has resulted in a reduced statistical power to address the potential impact of heterogeneity within the cohort.

INTRODUCTION

BRIGHTLIGHT is a programme of research which aims to determine whether specialist care for teenagers and young adults (TYA) with cancer is associated with improved outcomes. The National Institute for Health and Care Excellence (NICE) outlined in the *Improving Outcomes Guidance for children and young people with cancer* [1] a model of specialised care based on a limited number of hospitals designated as principal treatment centres (PTC). At that time minimal information was available about either the constituent parts of such specialist care or the benefits that might accrue from it and why. BRIGHTLIGHT comprises six interlinked projects centred upon a prospective, longitudinal cohort of young people recruited soon after a diagnosis of cancer that examines their outcomes and experiences of cancer care. Additional studies address elements of specialisation; the environment of care [2, 3]; the competencies desirable in healthcare professionals delivering specialist care [4]; a metric to quantify specialist care; caregiver's experience of care; and a health economic analysis to determine the cost of specialist care. The programme has been underpinned by an extensive patient and public involvement strategy [5-9].

Cancer in young people is uncommon, accounting for less than 1% of all new cancer diagnoses in England [10]. Despite its rarity, cancer is the second leading cause of death for young people, accounting for 11% of deaths in those aged 15-24 years [11, 12]. In addition, a number of issues argue for special attention for young people with cancer and for robust evidence to support current and future healthcare policies. For example, young people present with a spectrum of cancer types that is distinct from those affecting younger children and older adults [11]. A cancer diagnosis during adolescence and young adulthood has an acute and unique impact on this critical and complex stage of life development, disrupting physical health, social and educational goals as well as psychological wellbeing [13]. These

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factors have additional importance when considered against the advantages which accrue to society from the successful treatment through the prolonged fulfilment of their contribution in employment and other societal impacts [14].

While most young people are cured, outcomes for some cancers have not improved in line with those achieved for children and older adults [15]. There exists a general consensus among healthcare professionals that the needs of young people are poorly met by cancer services that are tailored towards the needs of children and older adults [16]. Young people fall between child and adult cancer services, into what has been described as either 'the grey zone' [17] or 'no man's land' [18]. Prolonged routes to diagnosis, unfavourable tumour biology with increasing age, limited access to clinical trials, lack of compliance with treatment protocols, inconsistent use of molecular diagnostics that may assist with optimal care, and a lack of specialist supportive care have all been implicated in the short fall in survival improvements [19-28].

Young people themselves have described unsatisfactory experiences of care which include: lack of recognition of their autonomy; failure to facilitate them to meet normal life goals during treatment; lack of peer support; care by staff with little experience of young people; and finally, inappropriate care environments [9, 29-31]. The inability of traditional healthcare silos to meet the unique psychosocial and healthcare needs of this specific population is increasingly highlighted [32-34]. Place of treatment and delivery of cancer care, in terms of both disease and age-appropriate specialist settings is increasingly acknowledged as potentially significant to the outcomes for young people with cancer [35, 36].

To address these unique needs and deficit in outcomes' knowledge, in August 2005 the NICE *Improving Outcomes Guidance* recommended that all care for patients under 19 must be provided in age-appropriate facilities and those aged 19 and over should have 'unhindered access to age-appropriate facilities and support when needed' [1]. To accommodate this recommendation thirteen TYA PTCs were identified across England. Key components of the services of the TYA PTC encompass tumour site-specific expertise delivered in conjunction with meeting the broader psychosocial needs of young people to support successful navigation of critical life transitions. This is directed through the TYA multi-disciplinary team (MDT) [1]. But, despite national guidance supporting this approach to the delivery of cancer care for young people aged 15-24 years [1]. around half of young people continue to be treated in children's and adult cancer units with no or limited access to the TYA PTC, many receiving care in hospitals 'designated' by NHS commissioners to provide elements of specialist care that are available in a TYA PTC.

The aim of the BRIGHTLIGHT programme of research is to evaluate the benefit of specialist TYA cancer services for young people aged 13–24 years. The study has four key objectives specific to the cohort:

1. Relate the proportion of care young people received in a TYA PTC to: quality of life, satisfaction with care, clinical processes and clinical outcomes
2. Examine young people's experience of cancer care through a longitudinal descriptive survey
3. Compare social and educational milestones amongst young people receiving different levels of TYA cancer care
4. Determine the costs of specialist care to young people, their families and the NHS

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Objectives

The aim of this paper is to describe the complex recruitment process for establishing the BRIGHTLIGHT cohort, provide details of bespoke measures of levels of care and disease severity that were developed to inform the analysis of the evaluation, and to describe the baseline characteristics of the cohort.

STUDY DESIGN

The BRIGHTLIGHT cohort is a prospective longitudinal cohort study, obtaining data through a bespoke survey, administered through face-to-face interview, telephone interview and online, five times over three years: 5-7 months after diagnosis then at 12, 18, 24 and 36 months [37].

PATIENT AND PUBLIC INVOLVEMENT

The focus of this study was identified by young people as a priority area for research. BRIGHTLIGHT was preceded by a period of feasibility work where we worked with young as co-researchers to develop the research questions, outcome measures and study design [6, 9]. The study has a Young Advisory Panel who have worked with us since 2011, who have been integral in naming the study [5], study management [7, 8], identifying other areas for research [38] and dissemination [39].

SAMPLE AND SETTING

Participants

The BRIGHTLIGHT cohort included young people aged 13-24 years, newly diagnosed with cancer (ICD-10 codes C00-C97) in an English hospital and recruited within four-months of diagnosis. Eligibility criteria were as inclusive as possible so no restriction according to language or a sensory impairment that affected communication was applied. The only exclusion criteria were: young people receiving a custodial sentence; if the young person was not anticipated to be alive at the first point of data collection (6-months after diagnosis); recurrence of a previous cancer or they were not capable of completing a survey, e.g. sedated and in intensive care.

Recruitment

Young people present with a wide range of cancer diagnoses [11]. It was anticipated that to identify and recruit potentially eligible patients would be the biggest challenge because of: 1) low incidence 2) presenting to numerous points in healthcare system, due to age and multiple diagnostic subtypes; and 3) inconsistent referral pathways for tertiary care. The NICE guidance was issued in 2005 [1], and by 2010 only 40% of newly diagnosed young people were known to a TYA MDT based at a PTC [40]. Analysis of the national cancer datasets between 2010 and 2011 indicated that young people were being treated in an additional 133 hospitals across England. Thus, to capture the full cohort of young people we needed to open recruitment in as many hospitals as possible, have a mechanism to identify young people across the country and also have access to an extensive network of researchers to recruit and administer the study questionnaires.

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There were two mechanisms for identifying young people: first through the national Cancer Waiting Times (CWT) dataset, which has been reported in detail previously [41]. This is routinely collected NHS data used to monitor diagnostic and treatment targets; feasibility work suggested young people could be identified within three months of diagnosis [42]. However, when this method was applied nationally it was found to be neither timely nor accurate so a second mechanism was introduced: Principal Investigators were asked to liaise with the coordinators of all tumour-specific MDTs (except prostate cancer) so the person managing recruitment to the study could be informed of new diagnoses in young people aged 13-24 years. A third method to directly approach young people to invite them to participate was also introduced in the later stages of recruitment but did not significantly impact on accrual [43].

The second challenge was working with a very large number of hospitals, of which most were likely to identify a few eligible patients over the course of the study and who might present to one of several departments. BRIGHTLIGHT opened to recruitment in 109 hospitals, of whom 97 identified and recruited between 1-106 (median 5) young people per hospital, 12 not recruiting any participants. England has a national network of research personnel funded by the National Institute for Health Research (NIHR), tasked with facilitating recruitment into clinical studies [41]. The aim was to recruit 2,012 young people diagnosed between July 2012 and December 2013. Despite making multiple targeted amendments to the protocol and iteratively working with NIHR researchers and the TYA healthcare professional community to increase the proportion of patients who were offered study entry (supplemental file 1), recruitment was slower and lower than anticipated. In April 2014, an extension to recruitment until April 2015 was approved (young people diagnosed until December 2014, recruited within 4 months of diagnosis), and a lower target sample size was agreed (Figure 1).

Ethical approval and consent

The study was approved by London Bloomsbury NHS Research Ethics Committee (reference LO/11/1718). Approval by the Secretary of State under Regulation 5 of the Health Services (Control of Patient Information) Regulation 2002 was obtained from the Health Research Authority Confidentiality Advisory Group (reference ECC 8-05(d)/2011) to access the CWT dataset, Hospital Episode Statistic (HES) data and data from the National Cancer Registration and Analysis Service (NCRAS).

METHODS

Data were collected from three sources: young people, patient medical records, and central NHS and Public Health England (PHE) databases.

Data from young people

Patient-reported outcomes were collected from young people at five time points over three years: 4-7 months after diagnosis (wave 1), 12 months (wave 2), 18 months (wave 3), 2 years (wave 4) and a final data capture 3 years after diagnosis (wave 5). Data were collected using a study-specific questionnaire, the BRIGHTLIGHT Survey [37] (available under licence from https://xip.uclb.com/i/healthcare_tools/brightlight_wave1.html), which was administered as a face-to-face interview in young people's homes at wave 1. Subsequent

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waves were administered online or through telephone interviews. At wave 1, young people also completed study-specific health economics questionnaires, described below.

The BRIGHTLIGHT Survey

The BRIGHTLIGHT Survey is an investigator and young person-designed self-report questionnaire that was administered through computer-assisted personal, telephone or web interviewing or web by an independent research organisation. It was developed utilising patient-experience literature [44] and was underpinned by a conceptual framework to guide question content [9]. The BRIGHTLIGHT Survey contains five validated outcome measures and questions to reflect young people's experience of diagnosis and cancer care (Table 1) [37]. Completion of treatment occurs at different time points according to diagnosis. During the feasibility work young people emphasised that they did not want to be asked questions about cancer when treatment ended and therefore the computer administration of the BRIGHTLIGHT Survey had complex routing to ensure young people were only asked questions that were relevant to their current situation [37]. For example, questions related to pre-diagnosis and diagnostic experience were only asked at wave 1. The BRIGHTLIGHT survey also utilised 'pull through' options so that participants could reflect on responses given in previous waves before answering. For example, questions about employment/education goals were tailored so participants could be asked again at wave 5 to ascertain if goals had changed and if this was cancer-influenced.

Table 1: Summary of the content of the BRIGHTLIGHT Survey

Construct and questionnaire	Details
Quality of life – Pediatric Quality of Life Questionnaire (PedsQL™) [45]	Contains 23 items scored on a 5-point Likert scale. Four domains: physical, emotional, social and work/school functioning. Two summary scores (physical and psychosocial function) and a total score. Domain, summary and total scores on 0-100 scale, with 100 representing the best possible quality of life. Scores <69.7 indicate a high risk of impaired quality of life [46].
Health status – Euroqol- 5 Dimension 3 level (EQ-5D-3L) [47]	Comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) scored on 3 levels (no, some, severe problems). The EQ visual analogue scale records self-reported health on a vertical scale ranging from 'best imaginable health state' to worst imaginable health state'. Scores 0-1 with 0 representing death and 1 perfect health (negative scores represent a health state worse than death).
Anxiety and depression – Hospital Anxiety and Depression Scale (HADS) [48]	A measure of depression and anxiety. Contains 14 items, scored on a four-grade scale (0 to 3). Summary scores for depression and anxiety (ranging from 0 to 21). Scores of 8-10 are defined as borderline and 11 and over are considered moderate/severe anxiety and depression [49].
Social support - Multi-dimensional Scale of Perceived Social Support (MSPSS) [50]	Scores for support by friends, family and significant others plus total support score. Contains 12 statements, rated on 7-point Likert scale. Total support score is an average ranging from 1-7, sub-support

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	scores range 4 – 28. Total scale score 1-2.9 are considered low support; a score of 3-5 is considered moderate support; and scores from 5.1-7 are considered high support.
Illness perception - The Brief Illness Perception Scale (BIPS) [51]	Measures the emotional and cognitive representations of illness. Contains eight* questions with fixed response scale specific for each question, e.g. not at all – extremely helpful. Each question represents a different dimension of illness perception: consequence, personal control, treatment control, timeline, identity, coherence, emotional representation, concern. Responses scored 1 – 10, the higher the score the greater perceived illness impact. No overall score and each question represents a single domain.
Cancer experience questions [37]	Comprises of 12 experience domains: pre-diagnosis experience, diagnostic experience, place of care, contact with healthcare professionals, treatment experience, fertility, involvement in clinical trials, adherence, communication and coordination of care, education, employment, wellbeing and relationships. Total of 238 questions with question specific responses describing experience

*Timeline statement not included

Health economics questionnaires

Cancer/treatment related costs incurred by young people and families were collected using a study-specific Cost of Care Questionnaire and Cost Record. These included questions regarding: travel (car parking, petrol and capital depreciation, public transport); time off work; medical equipment use; prescription and over the counter drug use; cost of accommodation incurred through hospitalisation; complementary and alternative medicine; and cost of family care for siblings. The Cost of Care Questionnaire was administered at wave 1 and required young people and their families to record costs incurred from the above items retrospectively since diagnosis. The Cost Record was given at waves 1 and 2, requesting the same information collected prospectively, on a weekly basis.

Data from medical records

Research teams who recruited young people completed an electronic Case Report Form (CRF) 12 months after diagnosis, which contained key variables relating to diagnosis, treatment, clinical process and outcome variables. This included postcode at the time of diagnosis, locations of care, details of diagnosis, MDT treatment planning and care, and outcomes at 12 months after diagnosis. The Index of Multiple Deprivation (IMD) is a measure of socioeconomic status [52] and was derived from the postcode at diagnosis, based on the population denominator of England. Clinical processes of care were defined as *documentation of*:

1. Histological diagnosis
2. Molecular diagnosis
3. Cancer stage or prognostic group
4. Initial treatment plan
5. Evidence of multidisciplinary communication

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6. Assessment by supportive care services, defined as documented contact with a Clinical Nurse Specialist plus one other member of the MDT (social worker, youth support coordinator, counsellor, psychologist, dietician, physiotherapist, occupational therapist)
7. Fertility discussion
8. Consideration for inclusion in a clinical trial

Data from national datasets

Data from NCRAS and HES were used to supplement and validate details of treatment received in the TYA PTC, to support a detailed health economic evaluation based on hospital attendance and healthcare received, and to cross check against the e-CRF. NCRAS data included date of diagnosis, tumour morphology, staging and treatment data; and HES data included dates for admitted patient care (APC), outpatient and accident and emergency attendance, plus receipt of chemotherapy and radiotherapy.

DEVELOPMENT OF BESPOKE METRICS

Defining levels of care

BRIGHTLIGHT aims to evaluate exposure to specialist TYA cancer services, defined as treatment in the TYA PTC. In recognition that patients may receive elements of care in more than one hospital, we proposed that care could be categorised by three levels according to the proportion of care received in a TYA PTC. To accurately allocate cohort participants to the appropriate level of care, analysis of HES data were used. In summary, PTC Trust codes were identified for 2012-2014 and applied to HES data so the proportion of days spent in a TYA PTC in the first 6 months and 12 months after diagnosis could be calculated (details provided in supplemental file 2).

Defining severity of illness

Advanced cancer is associated with poorer quality of life [53, 54]. We planned to compare quality of life of those treated in different care environments. To do so, we needed to consider ways to control for differences between patients which might influence this outcome and in particular, the severity of their cancer. However, this is difficult for TYA as they present with a heterogeneous array of malignancies [11]. While most cancers have staging criteria which differentiate between more or less extensive disease (typically groups 1-4 in ascending order of worsening survival), stage is not directly comparable between cancer types and a comparison based purely on staging would be meaningless due to the variation in outcomes between different cancers allocated to the same stage level. For example, stage 4 thyroid cancer is associated with a much higher chance of survival than say, stage 4 bowel cancer. Furthermore, survival alone is a good indicator of severity of illness as it takes no account of disease and treatment morbidity both for the short and long term. We therefore developed a bespoke 'severity' grading system to include symptom and treatment burden as well as predicted survival and burden of late effects. Each cancer type was graded as least, intermediate and most severe based on cancer-specific information thus allowing comparisons between groups of patients with multiple types of cancer (Table 2; detailed methodology is presented in supplemental file 3).

ANALYSIS

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The number of young people at each stage of the project were described using a flow diagram, including the numbers eligible, consenting to be involved, and followed up at each survey point. Reasons for non-participation at each stage were summarised. Potentially eligible patients who did not participate in the cohort study were compared against those who consented with regard to age, gender, ethnicity, location (based on the network linked to each PTC) and diagnosis. Data in both groups were summarised as means with standard deviations (sd), medians with interquartile ranges (IQR) or frequency and percentage (%), as appropriate and comparisons made using standard Chi squared and t-tests Since sample sizes for these comparisons were very large, statistical significance is defined as P<0.001. Survival from diagnosis was summarised using Kaplan Meier plots and the cohort and non-cohort groups compared using Cox regression to adjust for age, gender, ethnicity, location and type of cancer. Patient reported outcomes collected in the first wave were scored according to published guidance for each of the validated measures. The characteristics of the cohort were summarised using means/medians (sd/IQR) or frequency (%) as appropriate.

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Table 2: BRIGHTLIGHT Severity of Illness Index (see supplemental file 3)

Cancer type [11]	**Least severe**	**Intermediate severity**	**Most severe**
Germ cell tumours	Stages 1-3; Stage unknown	Stage 4 (stage 1S=stage 4)	
Leukaemias	CML	ALL; Other and unspecified	AML
Non-Hodgkin lymphoma and non-specified lymphoma	Over 16yrs, protocol unknown Stage 1-2	Over 16s, protocol unknown; Stage 3-4; Any paediatric-type protocol; All unknown	Burkitts (ICD10 C83.7, morphology code 9687/3)
Hodgkin lymphoma	All stages		
Central nervous system tumours	Pituitary adenomas (D35.2); Sub-ependymal giant cell astrocytoma (C43.2)	Other completely resected WHO grade I tumours for which surgery is the only treatment needed - except craniopharyngiomas	Craniopharyngiomas; incompletely resected or unresectable grade I tumours; all grade II-IV tumours, any needing radiotherapy or chemotherapy. This includes ependymomas, medulloblastomas and intracranial GCTs
Bone tumours	Surgery only (low grade, periosteal, parosteal)		All other
Soft tissue sarcoma	Stages 1-2	Stage 3; Unknown	Stage 4
Rhabdomyosarcoma	Low risk EpSSG A-D[1]		All others; Unknown
Melanoma	Stages 1-2 (except 2c)	Stage 2c; Stage 3 (except 3c); Stage unknown	Stage 3c; Stage 4
Carcinoma	All thyroid; All Stage 1; Cervix stage unknown	Stages 2-3; All nasopharyngeal; Stage unknown (except cervix)	Stage 4
Miscellaneous and unspecified		All	

[1] EpSSG: European Paediatric Soft Tissue Sarcoma Study Group

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RESULTS

A total of 1,126 young people were recruited for whom valid consent was available from 1,114 (Figure 2). Recruiting hospitals were required to keep a screening log, which was returned to the BRIGHTLIGHT team by 95 (87%) hospitals when recruitment ended. Of the 2,900 young people who had been screened, 429 (15%) were reported as not being eligible and 1,877 (65%) were eligible to participate. No details were provided for the remaining 594 (20%). Only 426 (23%) of those eligible had refused to participate, which was lower than the 35% we had anticipated and accounted for [8]. Of the 15% recorded as being ineligible, just over half (225, 52%) had either no reason recorded or appeared to have been deemed to be ineligible incorrectly.

Data were obtained from NCRAS for young people diagnosed in the same time period, who were potentially eligible, i.e., alive 6-months after diagnosis and place of residence was not linked to a prison postcode. A total of 5,953 young people were diagnosed with cancer between July 2012 and December 2014, of whom 5,835 (98%) were potentially eligible to participate[1]; 1,114 (19%) appeared in the BRIGHTLIGHT Cohort.

Clinical and NHS data were available for all 1,114 young people. Of these, 830 (75%) completed the wave 1 survey (Figure 2). In total, 163 (20%) participated once, 186 (22%) twice, 195 (24%) completed three, 173 (21%) completed four and 113 (14%) took part in every wave.

Non-participants were similar in age and ethnicity to those in the BRIGHTLIGHT cohort but there were differences in gender (a lower proportion of males in non-participants) and inclusion by tumour type (a greater proportion of young people with leukaemia and lymphoma, germ cell tumours and bone tumours compared to non-participants but lower representation of brain tumours, skin cancers and carcinomas) (Table 3).

Table 3: Comparison of characteristics of participants and non-participants

		N	BRIGHTLIGHT Cohort	N	Non-Participants	P-values[3]
Age at Diagnosis (years)	Mean (SD) Median (IQR)	1114	20.13 (3.28) 20.64 (17.58, 22.95)	4721	19.94 (3.33) 21 (17, 23)	0.08
Gender	Male Female	1114	618 (55%) 496 (45%)	4721	2213 (47%) 2508 (53%)	<0.0001
Ethnicity	White Asian Black Chinese Mixed Other	1085	936 (86%) 82 (8%) 22 (2%) 4 (<1%) 26 (2%) 15 (1%)	4316	3643 (84%) 288 (7%) 156 (4%) 34 (<1%) 74 (2%) 121 (3%)	0.002
Type of cancer[1]	Leukaemia Lymphoma CNS	1114	145 (13%) 350 (31%) 46 (4%)	4721	300 (6%) 781 (17%) 735 (16%)	<0.0001

[1] 109 young people died within 6-months of diagnosis so were assumed to be too sick to be approached and nine were in prison.

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	Bone		102 (9%)		177 (4%)	
	Sarcomas		78 (7%)		207 (4%)	
	Germ cell		212 (19%)		504 (11%)	
	Skin		45 (4%)		709 (15%)	
	Carcinoma (not skin)		125 (11%)		1210 (26%)	
	Miscellaneous specified		9 (<1%)		55 (1%)	
	Unspecified malignant		2 (<1%)		43 (1%)	
Geographical location[2]	Birmingham	1114	155 (14%)	4618	459 (10%)	<0.0001
	Bristol		116 (10%)		351 (8%)	
	Cambridge		23 (2%)		276 (6%)	
	Manchester		103 (9%)		391 (8%)	
	Merseyside		42 (4%)		239 (5%)	
	East Midlands		135 (12%)		278 (6%)	
	Leeds		106 (10%)		254 (6%)	
	Newcastle		59 (5%)		305 (7%)	
	Oxford		19 (2%)		249 (5%)	
	London (south)		77 (7%)		668 (14%)	
	Sheffield		37 (3%)		174 (4%)	
	Southampton		83 (8%)		221 (5%)	
	London (north)		159 (14%)		753 (16%)	

CNS: central nervous system; SD: standard deviation; IQR: interquartile range

[1] Based on the Birch classification [11]

[2] Hospitals mapped to the multidisciplinary team at the Teenage and Young Adult Principal Treatment Centre they were linked to

[3] P-values from Chi squared tests and t-tests as appropriate.

Of the 1,114 young people in the BRIGHTLIGHT cohort, 618 (55%) were male, mean age at diagnosis was 20.13 years (SD 3.28) and 936 (86%) identified themselves as white. Lymphoma was the most common cancer type (n=350; 31%), followed by germ cell tumours (n=212; 19%) and leukaemia (n=145; 13%) (Table 3). Table 4 details the sociodemographic and clinical characteristics of the BRIGHTLIGHT cohort. There was an even distribution across socioeconomic groups. Most were single (n=606; 84%) and employed or in education (n=531; 64%). Systemic anti-cancer therapy was the most common form of treatment, used for 880 (79%). Thirty (3%) young people received no treatment, just active monitoring. The clinical processes that were most frequently documented in the clinical records were MDT communication (n=1037; 97%), cancer stage or prognostic group (n=1015; 94%), histology (n=974; 91%) and initial treatment plan (n=974; 91%). One hundred and sixty seven (20%) young people reported having a pre-diagnosis long-term condition.

Table 4: Socio demographic and clinical characteristics of the BRIGHTLIGHT Cohort

Characteristic		Number	%
Socioeconomic status (IMD quintile) (N=1088)	1 – most deprived	250	23
	2	194	18
	3	209	19
	4	230	21
	5 – least deprived	205	19
Marital Status (wave 1; N=725)	Married/civil partnership	26	4
	Cohabiting	93	13
	Single/divorced	606	84
Current status	Working full/part time	257	31

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(at wave 1; N=830)	In education	274	33
	Other work (apprentice/intern/voluntary)	17	2
	Unemployed	31	4
	Long term sick	126	15
	Not seeking work	125	15
Length of inpatient stay over 12 months (N=1070) days	Median (IQR)	25	9 to 74
Treatment (N=1114)[2]	Systemic anti-cancer therapy	880	79
	Radiotherapy	324	29
	Surgery	551	50
	Active monitoring	30	3
	Transplant (stem cell or bone marrow)	28	3
Severity of illness (N=1114)	Least	611	55
	Intermediate	254	23
	Most	249	22
Clinical processes of Care (documentation available in clinical records)	Histological diagnosis (n=1072)	974	91
	Molecular diagnosis (n=737)[3]	258	35
	Cancer stage or prognostic group (n=1078)	1015	94
	Initial treatment plan (n=1071)	974	91
	MDT communication (n=1074)	1037	97
	Assessment by supportive care services (n=1057)	563	53
	Fertility being discussed (n=1063)	693	65
	Consideration into a clinical trial (n=1057)	676	64

CNS: central nervous system; IMD: Index of Multiple deprivation; IQR: interquartile range

[1]Based on period of 12 months from diagnosis. Missing for 70 participants: 26 had no days in hospital after diagnosis (inpatient stay was before diagnosis date) and data were missing for 44

[2] N greater than 1114 reflects multiple treatment modalities for some diagnoses

[3] Where relevant, indicated as not relevant in 320

A total of 124 (11%) young people in the BRIGHTLIGHT cohort died before 31st December 2016. Results from Cox regression indicate that a survival benefit for non-BRIGHTLIGHT patients was maintained even after adjustment for age, gender, ethnicity and type of cancer; the risk of death was 34% higher for those in the BRIGHTLIGHT cohort compared with those not in the cohort. (Figure 3; hazard ratio estimate 1.34 (95% confidence intervals 1.09-1.68), p=0.01; table 5). There was no evidence that survival of cohort participants compared with non-participants differed by cancer type (P-value for interaction P=0.12).

Table 5: Comparison of survival between participants in the Cohort and non-participants[1]

Estimated cumulative survival probabilities by year from diagnosis (95% CI)		
	Non-participants	BRIGHTLIGHT cohort
1 year	0.98 (0.97, 0.98)	0.98 (0.97, 0.99)
2 years	0.95 (0.94, 0.96)	0.92 (0.91, 0.94)
3 years	0.93 (0.92, 0.94)	0.89 (0.87, 0.91)
4 years	0.92 (0.91, 0.93)	0.88 (0.85, 0.90)

CI: confidence intervals

Log rank test P value <0.0001

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[1]Non-participants were young people diagnosed in the same time frame as the BRIGHTLIGHT cohort identified by the National Cancer Registration and Analysis Service (NCRAS), who were not part of BRIGHTLIGHT

A summary of patient-reported outcomes recorded at wave 1 are presented in Table 6. Mean total quality of life, physical and emotional domain scores were <69.7 indicating that, on average, young people had some impairment to quality of life shortly after diagnosis [46]. This is particularly notable in terms of physical scores where the average was significantly below the threshold, by more than 10 points, for a clinically important difference [55, 56]. Forty percent of young people could be classified as 'cases' for anxiety and 22% for depression (borderline-severe) [49]. Young people reported high levels of support from friends (Multi-dimensional Scale of Perceived Social Support cut off >5) and moderate support from family and significant others (score 3-5) [50]. The Brief Illness Perception Scale results indicate that young people felt cancer had a moderate effect on their life but they perceived that treatment was extremely helpful. They perceived themselves as having experienced a moderate number of symptoms and believed they had a good understanding of their cancer. The majority rated their satisfaction with care as being excellent/good (n=777; 94%). Those aged 19-24 years seemed to have better physical and psychosocial quality of life compared to those aged 13-18 years at diagnosis. This older age group also reported more anxiety, lower social support, better perceived personal control but lower perceived emotional representation and concerns. According to diagnosis, young people with a solid tumour had better physical scores, perceptions of consequences and identity but less support from friends than those with a blood cancer. Finally, there was a noticeable trend for better total quality of life, physical and psychosocial scores for those with less severe disease and worse emotional score for the intermediate severity group. Young people with less severe disease had better perceived consequences and identify but satisfaction with care was highest in those with the most severe disease.

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Table 6: Summary of the wave 1 patient-reported outcomes

			Age		Diagnosis		Severity of illness		
Characteristic	**N**	**All patients N=830**	**13-18yrs N=302**	**19-24yrs N=528**	**Haematology N=373**	**Oncology N=457**	**Least N=461**	**Intermediate N=194**	**Most N=175**
PedsQL - mean (SD)									
Total score	829	66.20 (19.79)	64.14 (18.53)	67.39 (20.40)	64.59 (18.28)	67.52 (20.86)	70.67 (18.86)	61.55 (19.77)	59.57 (19.25)
Physical summary score	828	59.45 (27.72)	54.67 (26.75)	62.20 (27.91)	56.96 (25.04)	61.47 (29.58)	67.65 (25.49)	52.67 (26.63)	45.33 (26.95)
Psychosocial summary score		80.38 (18.45)	77.88 (18.27)	81.82 (18.42)	79.37 (18.49)	81.21 (18.41)	84.15 (16.75)	75.90 (19.82)	75.43 (18.98)
Emotional summary score		67.64 (22.76)	70.94 (21.83)	65.75 (23.07)	67.75 (21.68)	67.55 (23.62)	68.05 (23.09)	64.92 (23.15)	69.57 (21.21)
EQ-5D – mean (SD)	830	0.76 (0.24)	0.75 (0.23)	0.77 (0.24)	0.77 (0.22)	0.76 (0.25)	0.81 (0.21)	0.71 (0.26)	0.71 (0.24)
Total score									
- **median (IQR)**		0.80 (0.69-1)	0.80 (0.62-1)	0.81 (0.69-1)	0.80 (0.69-1)	0.80 (0.66-1)	0.85 (0.73-1)	0.73 (0.62-1)	0.75 (0.59-0.88)
HADS – mean (SD)[1]	830								
Anxiety score		6.89 (4.39)	6.14 (4.12)	7.32 (4.49)	6.79 (4.36)	6.98 (4.43)	7.23 (4.55)	7.01 (4.44)	6.14 (3.83)
- Borderline n (%)		160 (19%)	51 (17%)	109 (21%)	75 (20%)	85 (19%)	82 (18%)	44 (23%)	34 (19%)
- Moderate/severe n (%)		172 (21%)	48 (16%)	124 (23%)	70 (19%)	102 (22%)	106 (23%)	40 (21%)	26 (15%)
Depression score		4.62 (3.68)	4.45 (3.38)	4.71 (3.84)	4.84 (3.57)	4.43 (3.76)	4.31 (3.65)	5.16 (3.79)	4.81 (3.57)
- Borderline n (%)		120 (15%)	40 (13%)	80 (15%)	48 (13%)	72 (16%)	48 (10%)	40 (21%)	32 (18%)
- Moderate/severe n (%)		55 (7%)	16 (5%)	39 (7%)	26 (7%)	29 (6%)	32 (7%)	14 (7%)	9 (5%)
MSPSS – median (IQR)									
Total support	820	1.50 (1.08-2.25)	1.58 (1.17-2.33)	1.50 (1-2.08)	1.58 (1.08-2.25)	1.42 (1.08-2.17)	1.50 (1.08-2.25)	1.58 (1-2.25)	1.50 (1.17-2.08)
Support - friends	827	7 (4-11)	7 (4-12)	6 (4-10)	7 (4-11)	6 (4-10)	7 (4-10)	7 (4-12)	7 (4-10)
Support - family	827	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	4 (4-7)
Support – significant others	823	4 (4-8)	5 (4-9)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-9)	4 (4-7)
BIPS – median (IQR)	830								
Consequences		7 (4-8)	7 (5-8)	7 (4-8)	7 (5-8)	6 (4-8)	6 (4-8)	7 (5-8)	7 (6-9)
Personal control		6 (4-8)	6 (5-8)	5 (3-8)	6 (4-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Treatment control		10 (9-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (9-10)	10 (8-10)
Identity		5 (3-7)	6 (3-8)	5 (3-7)	6 (4-7)	5 (2-7)	5 (3-7)	6 (3-8)	6 (4-8)
Coherence		8 (7-10)	9 (7-0)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	9 (7-10)
Emotional representation		6 (4-8)	5 (3-7)	7 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (3-8)
Concern		6 (3-8)	5 (3-7)	7 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Satisfaction with care – n (%)	820								
Excellent/good		777 (95%)	284 (95%)	493 (95%)	358 (96%)	419 (94%)	433 (95%)	173 (91%)	171 (99%)

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Fair/poor/very poor		43 (5%)	16 (5%)	27 (5%)	15 (4%)	28 (6%)	23 (5%)	18 (9%)	2 (1%)

BIPS: Brief Illness Perception Scale; EQ-5D: Euroqol 5-Dimension; HADS: Hospital Anxiety and Depression Scale; IRQ: interquartile range; MSPSS: Multi-dimensional Scale of Perceived Social Support; PedsQL: Pediatric Quality of Life Questionnaire;SD: standard deviation

[1]Borderline = 8-10, moderate/severe = >11 [49]

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DISCUSSION

The BRIGHTLIGHT cohort is the first national, prospectively recruited cohort of teenagers and young adults with cancer. We are able to examine in detail the complexity associated with place of care, experience and outcome. This is made possible through the use of linked data from multiple sources so unlike other cohorts which rely solely on patient-reported outcomes [34, 54] or clinical data [32], a more comprehensive evaluation can be derived. Using national mandatory NHS datasets we have been able to calculate a more robust measure of time spent in specialist TYA care. Other data sources, such as secondary analysis of the National Cancer Patient Experience data is based on TYA PTC code at the time of participation [57], as such this reflects a single point in time and does not reflect experiences and outcomes for those who have exposure to both specialist and non-specialist care. Measuring exposure to a TYA PTC through analysis of HES data has enabled a more objective exposure variable to be developed. Similarly, defining severity of cancer through prognosis for survival alone does not reflect the symptom/treatment burden of disease and the impact this has on quality of life during treatment and recovery. Systematically defining prognosis alongside symptom and treatment burden, provides a more nuanced measure and is a better reflection of the severity of illness.

Selecting the study design to evaluate TYA cancer services across England was challenging as services were already in place and, in some regions of the country, long-established. There was also wide variation in implementing the NICE Guidance [1] according to local need and pre-existing resources, resulting in services at PTCs not being identical. The decision to establish a cohort was made on the basis that it is suited for investigating rare exposures, allows examination of multiple outcomes for the defined exposure (to specialist care), and would enable us to gather data regarding sequence of events, with the potential to assess causality. The main limitation of the cohort is we only recruited a fifth of the population who were eligible to participate. Variation in diagnosis and severity between those in the cohort receiving different level of PTC care reduces the potential to assess causality.

Cohort studies are acknowledged to be challenging to establish and maintain, especially in rare conditions due to the requirement for large numbers of subjects, potential for selection bias and the challenges associated with subject retention [58-61]. We anticipated that participation might favour those who were less unwell or had a better prognosis. The inclusion of significant numbers with tumours associated with poorer prognosis such as bone tumours and the inferior survival of the cohort go against this. One of the aims of the BRIGHTLIGHT was to evaluate socioeconomic variation in access to specialist care. A comparison of IMD quintile between those who were and were not recruited who have enabled us to assess whether there was bias in recruitment according to difference socioeconomic groups; however, these data were not available but warrant exploration in the future. Our experience of recruitment points to the value of maintaining accurate screening logs and seeking mechanisms to complement the intelligence from local teams about change of status of participants such as death or change of address.

Our experience highlights the value of patient and public participation in research. We have described earlier in the paper the involvement young people had from study inception to

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dissemination. In total more than 1,200 young people have been involved in BRIGHTLIGHT as part of the research process almost the same number as those recruited. We believe this has positively influenced the rates of participation, ways in which young people were approached and methods of data collection, and doubled the retention rate at Wave 3 [7].

This population is known to have lower involvement in clinical trials in comparison to children and older adults [22, 62], yet there have been no targeted interventions developed to improve recruitment [63]. We have reported that to optimise recruitment to clinical trials, what we have identified as 'the 5'A's' need to be addressed, namely availability, accessibility, awareness, appropriateness, and acceptability [62]. We have identified factors that young people feel are acceptable for accessing research [8] and for continuing their involvement in a study [7]. We have also identified that the networked structures for facilitating recruitment into cancer research in England may not be optimal for the recruitment of young people [41]. The impact of not having an optimal research network was made apparent through BRIGHTLIGHT, as it was the first national study in this population. Ways to overcome this challenge are currently being explored by the NIHR.

A potential limitation of the BRIGHTLIGHT cohort study is the outcome measures that were selected to be included in the survey. Traditionally outcome measures are developed for children less than 18 years or adults older than 18. Our population crossed both age groups so there were limited measures validated for use in this population. Our measure of quality of life, the PedsQL, has been validated for use in adolescence and adulthood [45] and has been used often in TYA cancer studies [34, 64-67]. The other measures, outlined in Table 1, had no formal psychometric testing specifically in a TYA cancer population. However, these have been used extensively in studies in young people with and without cancer [68-74] so we are confident the results reflect a consistent measure of each construct, but warrants further exploration of the data in the future.

FUTURE PLANS

The BRIGHTLIGHT cohort was originally designed to evaluate short-term outcomes, from early after diagnosis to three years after diagnosis, over five time points. Data collection for wave 5 ended in February 2018, with results for the four key objectives anticipated to be available by the end of 2018. As noted earlier, the study has generated a large quantity of data and with the recent completion of a James Lind Alliance Priority Setting Partnership exercise for TYA exercise (http://www.ncri.org.uk/ncri-blog/top-10-research-priorities-for-teenage-and-young-adult-cancer-identified/), there is the opportunity to address some of the unanswered questions with the BRIGHTLIGHT cohort. This opportunity has already been realised to contribute evidence to improvements in early diagnosis [19]. In line with NIHR guidance, patient-reported outcome data from the cohort will be made available to external researchers on acceptance of the final report in the NIHR Journal Library. Details of how to apply will be made available on the website (www.brightlightstudy.com).

The philosophy of specialist TYA cancer care is to provide optimal cancer treatment alongside the developmentally-sensitive care that enables young people to achieve their life goals (e.g. education, employment, relationships) during treatment and beyond. BRIGHTLIGHT will evaluate this in the short-term but longer-term follow-up may be valuable

to explore whether the model of care delivery influences these outcomes later in life. We are now planning a 10-year follow-up study to assess the long-term impacts. We also acknowledge that similar to other studies quantifying care using NHS data [57, 75], the measure of specialist care may lack discrimination, not least because it assumes that all TYA PTCs and other places of care are equal. Additional to the cohort, a case study was conducted to understand the culture of TYA cancer care [3]. There is the potential to synthesise the qualitative findings from the case study with the quantitative data from the cohort to develop a more detailed and sensitive metric to define specialist TYA cancer care. Ultimately, the data generated by the cohort and BRIGHTLIGHT will provide new information on cancer in young people and determine if access to a PTC adds value. The relationships between specialist care and outcomes have previously been unclear. Findings will inform intervention and policy efforts to improve outcomes for young people with cancer.

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RMT, LAF, JB, DS, SM, RF, LH, MM, FG, RR, JSW were involved in developing the protocol. RMT coordinated the running of the study and was responsible for data acquisition. JB, JGA, RMT, LAF, SM, RF, DS, JSW contributed to the analysis. RMT, LAF, JB and JSW drafted the manuscript. All authors critically revised and approved the final manuscript.

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None declared.

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Data sharing statement:
Further details of the BRIGHTLIGHT programme of work is available through the study website (www.brightlightstudy.com). Data that are not held under licence with Public Health England or NHS Digital will be available from late 2018 when the primary analysis is complete. We welcome collaboration, for general data sharing enquiries please contact RMT (rtaylor13@nhs.net).

After 2nd review

Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures

i. Open to most Trusts agreeing to participate (n=77); posters to advertise BRIGHTLIGHT distributed to all Trusts
ii. Information to all newly diagnosed young people distributed in CLIC Sargent information packs; top recruiters reported in the TYAC weekly bulletin (the professional organisation in the UK supporting healthcare professionals with adolescents and young adults with cancer)
iii. Healthcare professional information leaflets sent to all Trusts (hard copy and electronic for local distribution)
iv. Director/Assistant Directors of the National Cancer Research Network emailed all the Cancer Network Managers directing them to make recruitment to BRIGHTLIGHT a priority; approved amendment to allow consent to be taken the same time a giving the information sheet
v. Review of screening logs and site specific feedback presentations sent to each Principal Treatment Centre (PTC)
vi. Open to recruitment in all 13 PTCs
vii. Approval to use social media to recruit young people; open in all 109 Trusts agreeing to open to recruitment
viii. Attendance at a Teenage Cancer Trust Lead Nurse event to highlight recruitment issues and gain support
ix. Emails sent by universities (communication teams or student unions) to current students with a link to the website to capture young people continuing with education after diagnosis; training for Youth Support Coordinators to be able to recruit young people
x. Attend a CLIC Sargent Social Worker event to promote the study and gain support to take a recruitment role
xi. Information on the BRIGHTLIGHT website in video format
xii. Recruitment method based on the National Cancer Patient Experience Survey implemented

Figure 2: A summary of participation at each wave of data collection

* Drop outs between waves due to death, permanent opt-out or wave opt out. Wave opt-outs prior to being issued were not permanent opt-outs; participants could opt-out of a single wave but participate in subsequent waves; these cases were not removed from the cohort permanently

Figure 3: Comparison of survival between participants in the Cohort and non-participants[1]

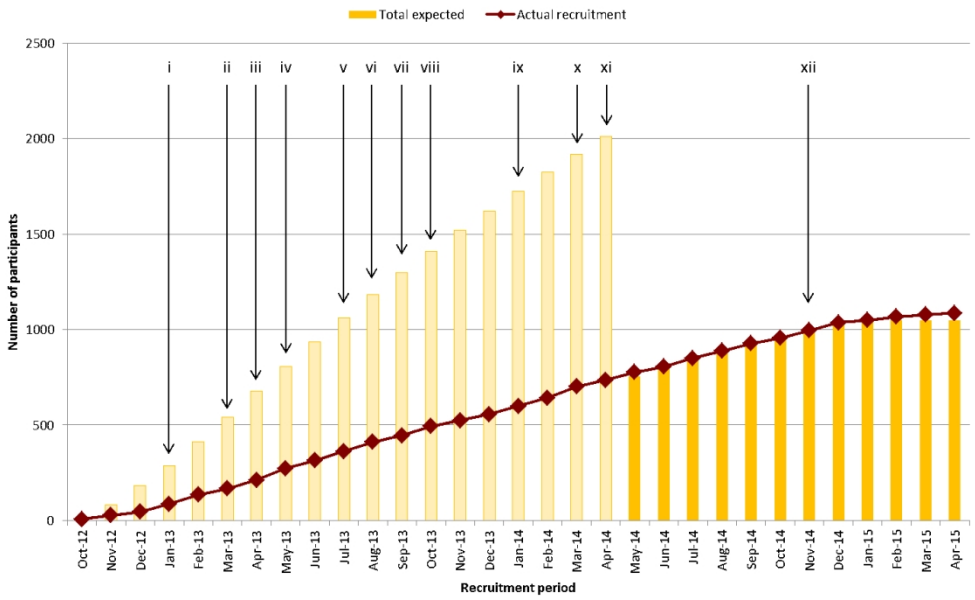
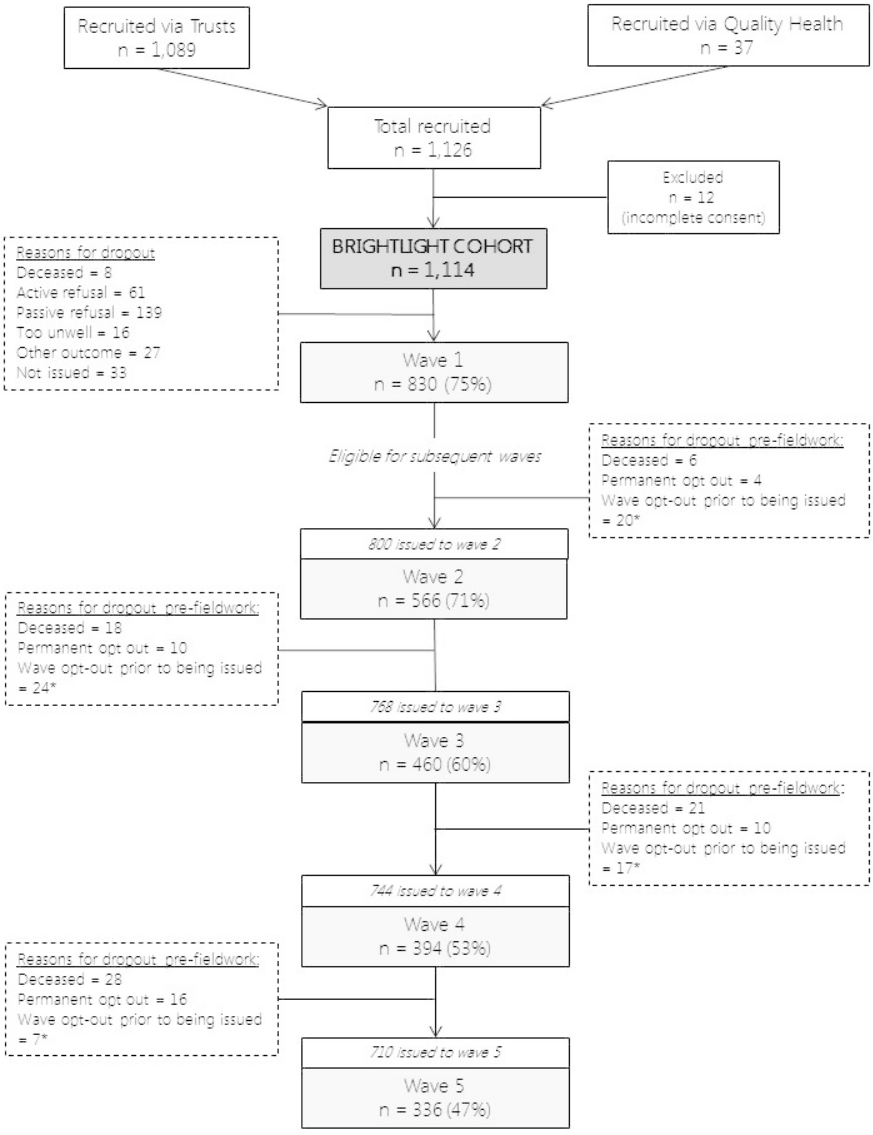


Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures



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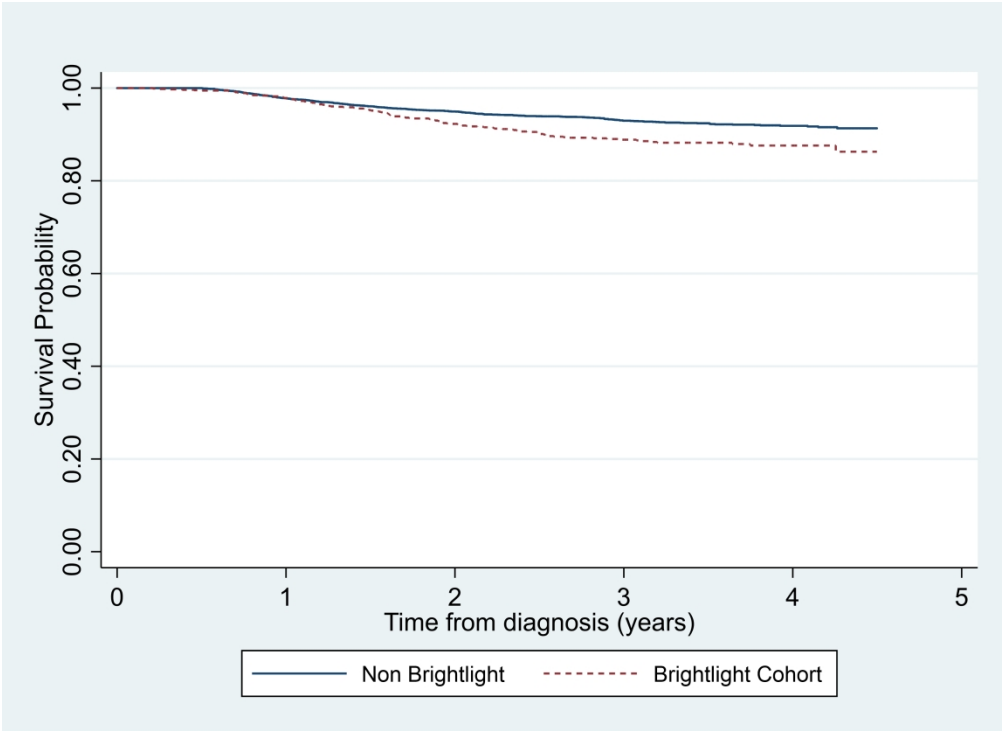


Figure 3: Comparison of survival between participants in the Cohort and non-participants

BRIGHTLIGHT Cohort profile – supplementary file 1

Supplementary File 1 Detailed results of actions implemented to improve recruitment to the cohort

Table A: Possible challenges reported by healthcare professionals before recruitment began and strategies identified to overcome them

	Challenges	**Strategies proposed to overcome challenges**
Identifying young people	Missing eligible young people if transferred to regional specialist centres Recruiting across a range of hospital sites Recruiting across multiple tumour types Engaging consultants: one concern was they would not think the older TYAs were eligible, a perception being that it was a 'teenager' study	Use the TYA MDT meetings to identify young people Co-ordination by a key person such as the Lead Nurse, cancer network head, or MDT lead to ensure details of eligible TYAs are passed to the recruiters Collaborative working with other centres to ensure all young people are approached, but not on multiple times
Approaching/consenting young people	Concerns about 'getting past' protective and upset parents Timing of consent, particularly if the patient is undergoing chemotherapy and was likely to be feeling very unwell Lack of experience in working with 'children' Being seen or felt to 'pressurise' potentially 'vulnerable and fragile' young people to take part Getting treating consultant approval to approach young people	Encouraging the initial approach to be a conversation, and not be immediately about persuading young people to take part Work with paediatric nurses to help with recruiting younger TYA Undertake paediatric consent training Wait for a sufficient length of time after diagnosis – maybe two months – before introducing the study, to allow the young person to become accustomed to the emotional and practical impact of the diagnosis

TYA: Teenage and young adult; MDT: multi-disciplinary team

BRIGHTLIGHT Cohort profile – supplementary file 1

Table B: Suggestions from healthcare professionals for keeping young people engaged throughout the study

Suggestion to keep young people engaged	**Action for implementation by BRIGHTLIGHT**
Get the consent process absolutely right: clear, accurate information about the survey, as buy-in from young people will increase the chances they will continue to participate	Information developed with young people, site initiation with recruiters to ensure they knew about the study and could relay information to young people in the best way
Provide TYA-friendly formats: e.g., ensure the survey could be completed on an iPad or iPhone as well as on a home computer	The survey was administered face-to-face at the first time point; subsequently it could be completed online on any platform
Use the internet: communicate via social networks like Facebook and Twitter	An open Facebook account was prohibited by the sponsor Trust but a Twitter account was opened
Ensure language used is aimed at empowering young people	All information was reviewed by the YAP[1] and had a reading ease of >70%
Consider incentives: e.g., a medal-based reward system – for each year young people remain in the study they move up the medals from Bronze (Year 1) to Silver (Year 2) and Gold (Year 3) and get a correspondingly increasingly valuable reward each time.	The YAP suggested a reward system using wrist bands with a different colour for each wave of participation
Inform participating young people on why the study matters and why their continuing involvement is important	A website was developed to keep young people updated about the programme www.brightlightstudy.com
Maintain contact throughout	Newsletters
Disseminate progress and results so they can see the wider scale and impact of the survey, that is making a difference	Content of newsletters related to results as far as was possible
Keep parents on board perhaps with targeted communications	Newsletters sent to all the email addresses provided
Distribute posters and flyers to treatment centres	Posters and flyers provided

YAP: Young Advisory Panel; TYA: teenage and young adult

[1]YAP are the BRIGHTLIGHT patient user group

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C: Suggestions for how the BRIGHTLIGHT Team might facilitate recruitment and actions taken to address these

Suggested change	Action by the BRIGHTLIGHT Team
1. Study information for health professionals	An information booklet was developed giving a brief summary of the study. This was sent electronically and as hard copies to all participating Trusts. Regular newsletters were developed and circulated online and as hard copies. Recruitment figures were circulated in a weekly Bulletin by TYAC to their members and were also Tweeted by the BRIGHTLIGHT team (@bR1GhTLiGhT)
2. Make the participant information sheets as short as possible	A summary booklet had been produced by Ipsos MORI[1] to send as a reminder about the study by their interviewers. An ethics amendment was made in July 2013 to allow this to be used in conjunction with the lengthy information sheet at the time of consent. Video versions of the information sheet were made available on the website (www.http://www.brightlightstudy.com/user-involvement/)
3. Investigate any variation in recruitment rates between sites	Screening logs were requested and analysed to identify reasons for suboptimal recruitment, which was fed back to each Trust with guidance on how to overcome recruitment issues.
4. Reduced interval between giving information and getting consent[2]	An amendment was approved by the Ethics Committee to allow consent to be taken within the same 24-hour period as information was given.
5. Provide BRIGHTLIGHT advertising materials	Posters, flyers and postcards had been available since the beginning of the study. These were distributed not only by the BRIGHTLIGHT Team but also by CLIC Sargent and Teenage Cancer Trust.
6. Keep sending the NWCIS notification[3]	There was a temporary pause in the CWT data being sent due to organisational change of NWCIS to Public Health England.
7. Extend the window of recruitment for wave 1	This was relaxed at the end of 2012 so young people could be recruited at any time in the first four months after diagnosis. We were unable to extend recruitment beyond this period because we wanted data to be collected within a specific time window. Young people were not able to enter the study at later time points because subsequent questions were informed by responses in the first survey.

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C. *cont.*

Suggested change	Action by the BRIGHTLIGHT Team
8. Reduce the number of times young people need to participate (total study participation involved 5 time points in 3 years)	The sample size calculation was based on participation at three time points (as specified in the protocol) because we were aware young people might opt in and out of participation depending on their current life commitments. We developed top tips for recruiting Trusts, including information about participation. The top tips were prominent on the website, were sent as an information leaflet, and included in the newsletter.
9. Enable information sheets to be posted to young people	An ethics amendment was approved to enable information sheets and consent forms to be posted and/or returned through the mail.
10. Make presentations at local network and Trust meetings	Members of the BRIGHTLIGHT team presented recruitment updates at every available national meeting. Trusts were also informed that the team would come to any local meetings on request. Site specific slides to present at MDTs were provided to all PTCs.
11. First survey to be online or telephone rather than face-2-face	This request could not be accommodated. A single mode of administration had been developed for the first survey.[4]

CWT: Cancer Wait Time database; MDT: multi-disciplinary team; NWCIS: North West Cancer Intelligence Service (after the move to Public Health England became known as the North West Knowledge Intelligence Team). PTC: Principal Treatment Centre; TYAC: Teenagers and Young Adults with Cancer (the organisation representing healthcare professionals working in this area).

[1] Ipsos MORI were the commercial company administering the BRIGHTLIGHT Survey; [2] Ethics guidance in the United Kingdom recommends a minimum of 24 hour between providing information and gaining consent to give participants time to process information; [3] NWCIS sent a monthly email to a dedicated person in each recruiting trust with a list of potentially eligible patients identified through the Cancer Waits dataset as newly starting treatment; [4]Subsequent waves had a choice of online or telephone interviewer administered survey; the online option has only been selected by a minority of young people

BRIGHTLIGHT Cohort profile – supplemental file 2

Supplemental file 2: Method for calculating the TYA Cancer Specialism Scale (TYA CSS) to assign level of care

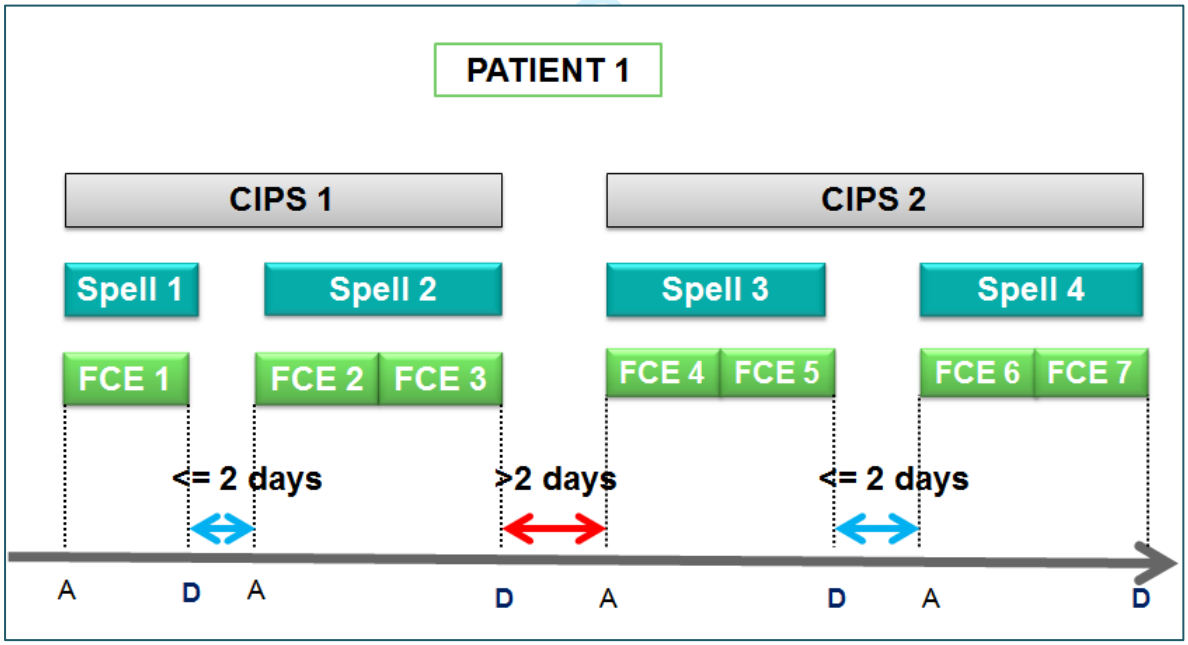
The TYA CSS is derived from admitted patient care data using linked Hospital Episode Statistic (HES) data. HES data from 2011/12 to 2016/17 were obtained from NHS Digital and linked to patients from the BRIGHTLIGHT cohort using the following identifiers: NHS Number, sex and postcode. The method for calculating the TYA CSS is adapted from an approach first proposed by Birch in 2013[1].

Hospital activity within HES is recorded in three ways (Figure 1):

1. Finished consultant episodes (FCEs)
2. Spells (sequential hospital encounters with different consultants)
3. Continuous inpatient spells (CIPS: hospital admissions for the same patient receiving care from different consultants and different providers/trust within two days after discharge)

FCE is the standard measurement unit for hospital activity and considered to provide more accurate estimates of consultant workload and hospital resources[2]. FCE was used for the basis of analysis and derivation of the TYA CSS to ensure we used all available data on consultant care at the deepest level of granularity available.

Figure 1: Different classifications of hospital admission for an example patient based on HES



Abbreviation: FCEs -finished consultant episodes, CIPs -continuous inpatient spells, A-admission, D- discharge.
Source: Analysing Patient-Level Data Using Hospital Episode Statistics (HES), University of York.

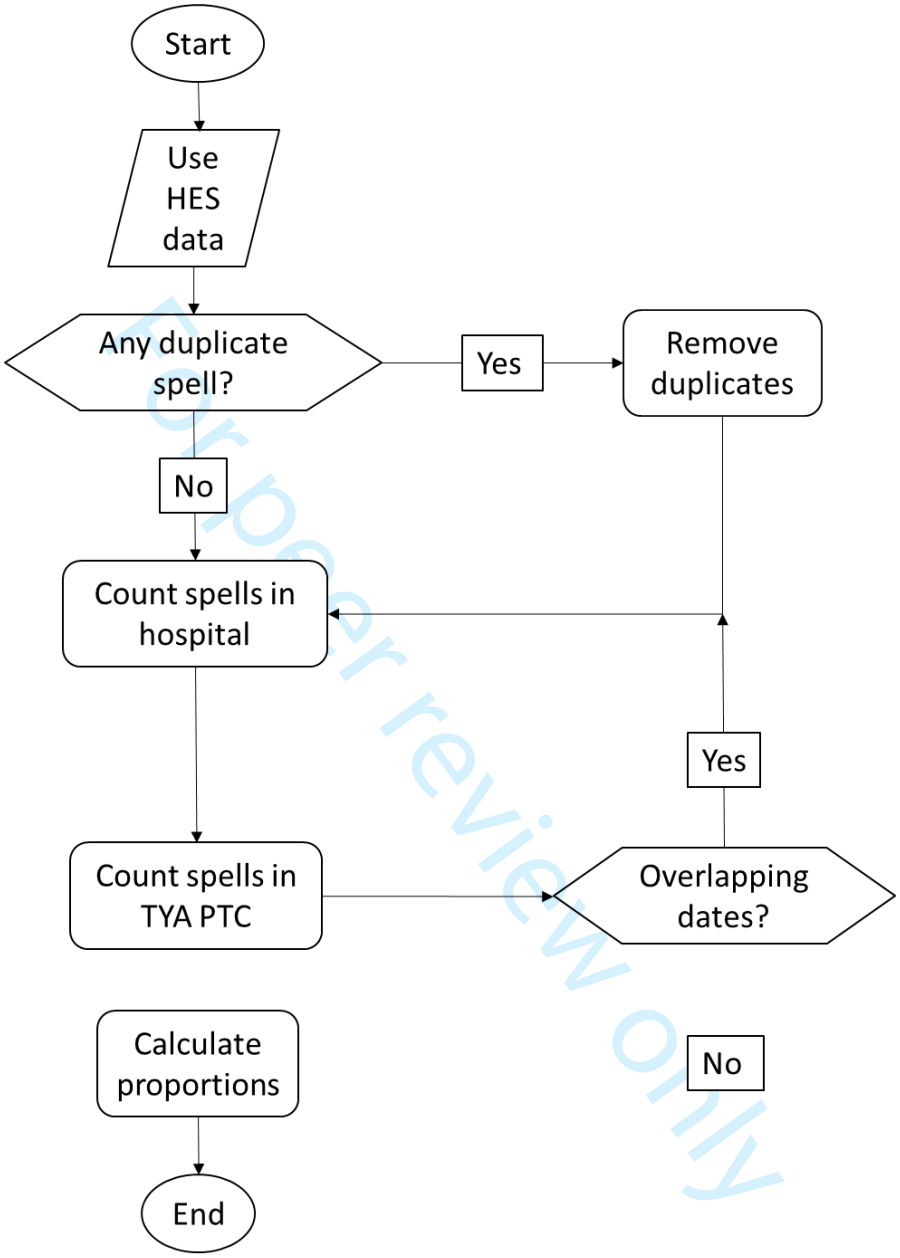
[1] Birch RJ. Teenage and young adult cancer in England – the patient journey and experience. The University of Leeds, PhD Thesis 2013

[2] Hargreaves DS, Viner RM. Adolescent inpatient activity 1999–2010: analysis of English Hospital Episode Statistics data. Archives of disease in childhood 2014; 99: 830-833

BRIGHTLIGHT Cohort profile – supplemental file 2

The development of the TYA CSS is summarised in Figure 2.

Figure 2: Summary of the process for calculating the TYA CSS



Data cleaning

HES data were cleaned to remove duplicates and to clarify some of the diagnostic coding. Reference was made to the HES admitted patient care data dictionary[3] to guide the data cleaning process in order to ensure accuracy and consistency in the recording and analysis of the HES records.

Duplicates were removed to ensure there were not several copies of the same admission being recorded for the same patient. These were identified by ascertaining whether more

[3] HSCIC. HES data dictionary. HEALTH AND SOCIAL CARE INFORMATION CENTRE 2016, 20 January 2016; Available from: http://www.hscic.gov.uk/hesdatadictionary

than one admission began on the same date for a single patient and then cross checking this against admission reasons, procedure codes and treating physician code. Examples of fields which would be indicative of duplicate admission records include multiple HES_IDs, episode start date, episode end date, admission date and discharge date.

Location of specialist care centres

The aim of the study is to evaluate the value of specialist cancer services. 'Specialist' was originally defined in the *Improving Outcomes Guidance (IOG)*[4] as 13 principal treatment centres (PTCs) across England. To account for the age range of the BRIGHTLIGHT cohort starting at 13 years, PTCs also included children's PTCs where the age of admission for the TYA PTC did not include younger adolescents (Table 1). The hospital codes for the look up tables were taken from NHS Digital[5].

Calculation of the scale

The level of specialist care received was calculated from the time of diagnosis (taken from the date recorded in the National Cancer Registration and Analysis Service dataset)

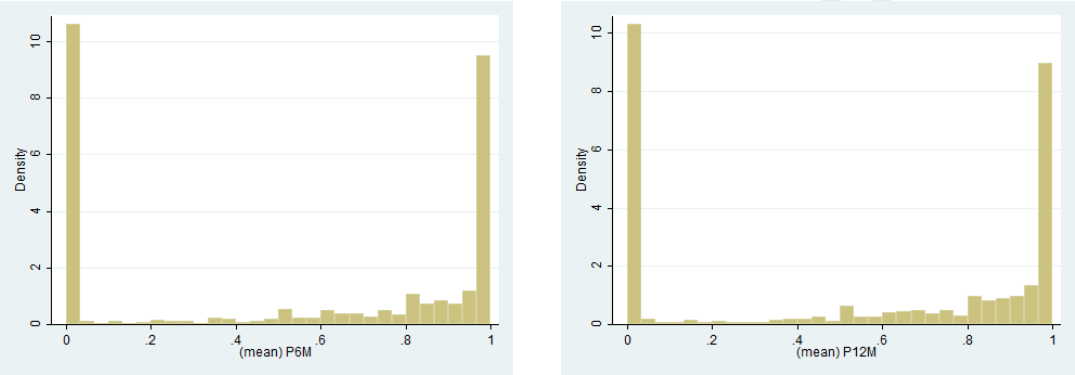
1. Six months after diagnosis: Spells in TYA PTC from diagnosis at 6 months/Total spells from diagnosis at 6 months
2. 12 months after diagnosis: Spells in TYA PTC from diagnosis at 12 months/Total spells from diagnosis at 12 months

For every individual, HES data were used to calculate the number of inpatient and day case bed days spent in a specialist centre (A), as well as the number of total bed days across all secondary care services (B) within the first 6 and 12 months after diagnosis. The proportion of time spent in a specialist centre was then derived as (A)/(B).

Defining the levels of care

Inpatient HES data were successfully linked to 1,074 out of 1,114 young people recruited to BRIGHTLIGHT. The distribution of the proportion of care by 6 months and 12 months after diagnosis suggested there were three natural groups occurring within the data (Figure 3).

Figure 3: Distribution of the proportion of care receive in a TYA PTC



[4] National Institute for Health and Care Excellence. Guidance on cancer services: improving outcomes in children and young people with cancer. NICE, London 2005https://www.nice.org.uk/guidance/csg7/resources/improving-outcomes-in-children-and-young-people-with-cancer-update-773378893 [Accessed 30/08/18]

[5] https://digital.nhs.uk/services/organisation-data-service

BRIGHTLIGHT Cohort profile – supplemental file 2

Table 1: List of principal treatment centres in England (2012-2014) for young people aged 13-24 years

Principal Treatment Centre	**Hospital**
Cambridge University Hospitals NHS Foundation Trust	Addenbrookes Hospital (aged 14-24)
The Christie NHS Trust	Christie Hospital (aged 16-24)
Manchester University Hospitals NHS Foundation Trust	Royal Manchester Children's Hospital (aged 13-15)
Clatterbridge Centre for Oncology NHS Foundation Trust	Clatterbridge Centre (aged 16-24)
Alder Hey Children's NHS Foundation Trust	Alder Hey Children's Hospital (aged 13-19)
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Royal Liverpool Hospital
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Broadgreen Hospital
Leeds Teaching Hospitals NHS Trust	Leeds General Infirmary (aged 13-16)
Leeds Teaching Hospitals NHS Trust	St James's University Hospital (aged 17-24)
Nottingham University Hospitals NHS Trust	City Campus (aged 18-24)
Nottingham University Hospitals NHS Trust	Queens Medical centre (aged 13-18)
Sheffield Teaching Hospitals NHS Foundation Trust	Weston Park Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Royal Hallamshire Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Sheffield Children's Hospital (aged 13-16)
Southampton University Hospitals NHS Trust	Southampton General Hospital (aged 16-24)
Southampton University Hospitals NHS Trust	Southampton Children's Hospital (aged 13-15)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Northern Centre for Cancer Care (aged 19-24)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Royal Victoria Infirmary (aged 13-18)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Sutton (aged 13-24)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Fulham (aged 17-24)
University College London Hospitals NHS Foundation Trust	University College Hospital (aged 13-24)
University College London Hospitals NHS Foundation Trust	Cancer Centre (aged 13-24)
University Hospital Birmingham NHS Foundation Trust	Queen Elizabeth Hospital (aged 16-24)
Birmingham Children's Hospital NHS Trust	Birmingham Children's Hospital (aged 13-18)
University Hospital Bristol NHS Foundation Trust	Bristol Haematology & Oncology Centre (aged 17-24)
University Hospital Bristol NHS Foundation Trust	Royal Hospital for Children (aged 11-16)
University Hospital Bristol NHS Foundation Trust	Bristol Royal Infirmary
University Hospital Bristol NHS Foundation Trust	St Michael's Hospital
University Hospitals of Leicester NHS Trust	Leicester Royal Infirmary (aged 13-24)
Oxford University Hospital NHS Trust	Churchill Hospital (aged 18-24)
Oxford University Hospital NHS Trust	John Radcliffe Children's Hospital (aged 13-18)

BRIGHTLIGHT Cohort profile – supplemental file 2

Supplementary File 2: Development of the BRIGHTLIGHT Severity of Illness Index (BRIGHTLIGHT SIX)

Rationale for developing a bespoke severity index

Within the BRIGHTLIGHT cohort, place of care was not randomly assigned but instead determined by local pathways of care, key influences including the type of cancer, age, proximity to principal treatment centres. As a consequence, differences exist between those who have all/some of their treatment in the teenage and young adult (TYA) Principal Treatment Centre (PTC) and those who have had no care in a TYA PTC. This fundamental difference between the populations of patients who receive no, some or all TYA PTC care was thought likely to be a major confounder in the interpretation of any observed differences in patient experience and outcome between these groups. The differences may not be reflected accurately if cases were grouped solely by, say, tumour type or disease stage due to the considerable variation between tumour types and between similar tumours of different stages in the intensity of treatment received and the likelihood of survival. To interpret the significance of any observed differences in our primary or secondary outcome measures across the populations with no, some or all TYA PTC care, we needed a measure that would allow comparison across patients with different tumours, but capable of discriminating between patient populations. Our primary outcome was quality of life (QOL) and a powerful determinant of QOL is 'the burden of cancer' patients had at diagnosis[1]. We wished to consistently and systematically describe the burden of cancer to assist analysis. The severity of illness index therefore needed to reflect prognosis, disease morbidity (symptoms, physical impact) and treatment morbidity (determined by treatment duration, intensity and anticipated late morbidity burden).

The BRIGHTLIGHT Severity of illness index (SIX)

Constructing the index

All cancer types were compared by symptom burden, treatment burden and prognosis using germ cell tumours as a reference: Stage 1 – very likely to survive, treatment either surgery alone or surgery plus a limited burden of chemotherapy, few if any anticipated late effects of treatment; Stage 2-3 – ~90% survival, many have intensive or multimodality treatment or larger operations, some late toxicity burden; Stage 4 – 50% survival and intensive treatment. Stage 4 we classed as 'most severe' and used this as a reference point to compare odds of survival and treatment burden for other cancers.

Germ cell tumours were chosen as a reference because they are relatively common in the TYA age group, have a range of prognoses from excellent to poor, and treatments have a range of morbidity from surgery alone through to very intensive chemotherapy with both acute and long-term sequelae.

[1] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

BRIGHTLIGHT Cohort profile – supplemental file 2

Three clinicians and two BRIGHTLIGHT researchers reviewed all cancer types to consider allocation to one of three severity levels. Survival estimates were based on examination of current or recently completed trial protocols where available and using a recently published comprehensive TYA-specific reference textbook[2]. We evaluated treatment burden using duration and expected toxicity from multiple sources, including clinical experience, trial protocols, a current TYA oncology text book and international guidelines (such as the National Comprehensive Cancer Network). In addition, other potentially comparable clinical severity scales were sought from the literature to determine comparability or utility in this context.

Content validity of the index

Once a preliminary scale had been constructed, its content was tested by expert review. At least two additional clinicians with specialist clinical expertise were approached to review each tumour type. The reviewers were sent a short document outlining the purpose of the scale and its development to that point as well as the scale itself. They were interviewed either face-to-face or by telephone by a senior clinician and BRIGHTLIGHT researcher (JSW) and asked to respond to two questions:

1. *Within the row(s) of the cancer types in which you have particular expertise (e.g. central nervous system tumours), do you agree with the allocation of grades of severity?*
2. *Looking at other tumour types, by comparison with other rows, do you agree with the allocation of grades of severity?*

Interviews were recorded and field notes taken. The scale was adjusted in response to expert comments to produce a final version (main paper, Table 2).

Applying the BRIGHTLIGHT SIX

BRIGHTLIGHT researchers (RMT, LAF, DS) independently allocated a severity level to each patient, conducting these assessments blind to responses to the survey, including QOL results. Comparisons between the three scores were made and, where there were differences, adjudication through a fourth researcher (JW) determined whether this was an error or due to ambiguity in the Index.

Other measures of severity

We found only one other example in which investigators had categorised TYA by cancer severity. Husson et al[1] used expected 5-year survival to divide patients into three groups, those with expected survival of greater than 80%, 50-80% and less than 50%.[3] Using the same source data[4], we also allocated each patient from the BRIGHTLIGHT cohort a second severity level based on 5-year survival.

We compared this method (Five year survival index, FYX) with BRIGHTLIGHT SIX. As anticipated, those judged to have the most severe cancer by BRIGHTLIGHT SIX are

[2] Bleyer, Barr, Ries, Whelan, Ferrari eds. Cancer in Adolescents and Young Adults. Springer International Publishing, Switzerland 2017

[3] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

[4] Bleyer, A. (2011). "Latest Estimates of Survival Rates of the 24 Most Common Cancers in Adolescent and Young Adult Americans." J Adolesc Young Adult Oncol 1(1): 37-42.

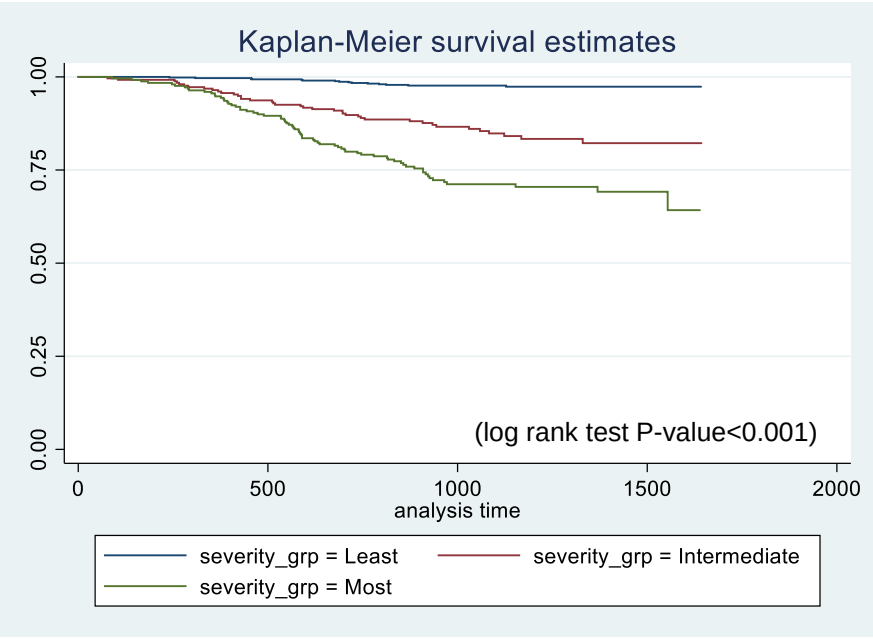
distributed across the three survival categories though weighted towards the two lower survival groups. Similarly, most but not all of those with the least severe cancer by BRIGHTLIGHT SIX had the best expected survival. Those with intermediate severity cancer are spread across the three FYX groups (Table 1).

Table 1: Comparison between the Five year survival Index (FYX) and BRIGHTLIGHT Severity of Illness Index (SIX)

	SIX level		
FYX	Least	Intermediate	Most
<50%	1	100	71
50-80%	56	98	171
>80%	546	56	7

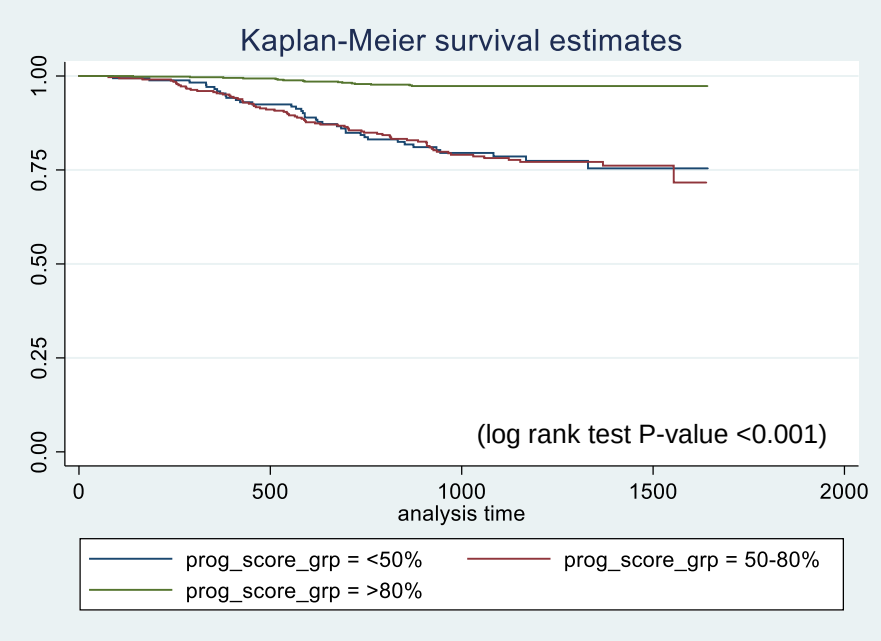
We then analysed survival of the BRIGHTLIGHT cohort using the two indices. Figure 1 demonstrated a clear discrimination in survival by BRIGHTLIGHT SIX, consistent with anticipated survival being an important but not sole component of the index. The survival of the BRIGHTLIGHT cohort was then examined by allocated FYX category (Figure 2). FYX failed to distinguish three groups with distinct survival as that of those allocated to the two lower categories was superimposed.

Figure 1: Survival by BRIGHTLIGHT Severity of Illness Index



BRIGHTLIGHT Cohort profile – supplemental file 2

Figure 2: Survival of BRIGHTLIGHT cohort against allocated FYX group



STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-9*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	Not applicable
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	Not applicable – only reporting baseline

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	characteristics
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 2
		(b) Give reasons for non-participation at each stage	Figure 2
		(c) Consider use of a flow diagram	Figure 2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	Tables 3-5
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable, presenting wave 1 data only
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable – wave 1 descriptive data only
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Descriptive data only presented
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Description of the BRIGHTLIGHT Cohort: the evaluation of teenagers and young adult cancer services in England

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Keywords:	BRIGHTLIGHT, Recruitment, Teenagers and Young Adults, Cancer, Observational Research, Cohort

After 2nd review

Description of the BRIGHTLIGHT Cohort: the evaluation of teenagers and young adult cancer services in England

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ABSTRACT

Objective: International recognition of the unique needs of young people with cancer is growing. Many countries have developed specialist age-appropriate cancer services believing them to be of value. In England, 13 specialist Principal Treatment Centres (PTC) deliver cancer care to young people. Despite this expansion of specialist care, systematic investigation of associated outcomes and costs has to date, been lacking. The aim of this paper is to describe recruitment and baseline characteristics of the BRIGHTLIGHT cohort, and the development of the bespoke measures of levels of care and disease severity, which will inform the evaluation of cancer services in England.

Design: Prospective, longitudinal, observational study.

Setting: Ninety-seven NHS hospitals in England.

Participants: A total of 1,114 participants were recruited diagnosed between July 2012 and December 2014: 55% (n=618) male, mean age was 20.1 years (SD=3.3), most (86%) were white and most common diagnoses were lymphoma (31%), germ cell tumour (19%) and leukaemia (13%).

Results: At diagnosis, median quality of life score was significantly lower than a published control threshold (69.7 points); 40% had borderline-severe anxiety, and 21% had borderline-severe depression. There was minimal variation in other patient-reported outcomes according to age, diagnosis or severity of illness. Survival was significantly worse in the Cohort than for young people diagnosed during the same period who were not recruited (cumulative survival probability 4 years after diagnosis: 88% vs. 92%).

Conclusions: Data collection was completed in March 2018. Longitudinal comparisons will determine outcomes and costs associated with access/exposure to PTCs. Findings will inform international intervention and policy initiatives to improve outcomes for young people with cancer.

After 2nd review

Strengths & limitations of this study

5 bullet points

- A cohort of teenagers and young adults with newly-diagnosed cancer was established with the involvement of young people in planning and operation which contributed to a high rate of retention.
- The socio-demographic characteristics of the cohort are broadly similar to the contemporary teenage and young adult cancer population, supporting the generalisability of results.
- Data has been collected from multiple sources including patients, individual clinical care records, and established National Health Service datasets.
- The study recruited a much smaller proportion of young people diagnosed with cancer in the available time period, resulting in lower statistical power to address the impact of heterogeneity..
- A metric developed to quantify specialist care may not be sensitive enough to reflect the complexity of specialist care and individual patient pathways.

INTRODUCTION

BRIGHTLIGHT is a programme of research which aims to determine whether specialist care for teenagers and young adults (TYA) with cancer is associated with improved outcomes. The National Institute for Health and Care Excellence (NICE) outlined in the *Improving Outcomes Guidance for children and young people with cancer* [1] a model of specialised care based on a limited number of hospitals designated as principal treatment centres (PTC). At that time minimal information was available about either the constituent parts of such specialist care or the benefits that might accrue from it and why. BRIGHTLIGHT comprises six interlinked projects centred upon a prospective, longitudinal cohort of young people recruited soon after a diagnosis of cancer that examines their outcomes and experiences of cancer care. Additional studies address elements of specialisation; the environment of care [2, 3]; the competencies desirable in healthcare professionals delivering specialist care [4]; a metric to quantify specialist care; caregiver's experience of care; and a health economic analysis to determine the cost of specialist care. The programme has been underpinned by an extensive patient and public involvement strategy [5-9].

Cancer in young people is uncommon, accounting for less than 1% of all new cancer diagnoses in England [10]. Despite its rarity, cancer is the second leading cause of death for young people, accounting for 11% of deaths in those aged 15-24 years [11, 12]. In addition, a number of issues argue for special attention for young people with cancer and for robust evidence to support current and future healthcare policies. For example, young people present with a spectrum of cancer types that is distinct from those affecting younger children and older adults [11]. A cancer diagnosis during adolescence and young adulthood has an acute and unique impact on this critical and complex stage of life development, disrupting physical health, social and educational goals as well as psychological wellbeing [13]. These factors have additional importance when considered against the advantages which accrue to society from the successful treatment through the prolonged fulfilment of their contribution in employment and other societal impacts [14].

After 2nd review

While most young people are cured, outcomes for some cancers have not improved in line with those achieved for children and older adults [15]. There exists a general consensus among healthcare professionals that the needs of young people are poorly met by cancer services that are tailored towards the needs of children and older adults [16]. Young people fall between child and adult cancer services, into what has been described as either 'the grey zone' [17] or 'no man's land' [18]. Prolonged routes to diagnosis, unfavourable tumour biology with increasing age, limited access to clinical trials, lack of compliance with treatment protocols, inconsistent use of molecular diagnostics that may assist with optimal care, and a lack of specialist supportive care have all been implicated in the short fall in survival improvements [19-28].

Young people themselves have described unsatisfactory experiences of care which include: lack of recognition of their autonomy; failure to facilitate them to meet normal life goals during treatment; lack of peer support; care by staff with little experience of young people; and finally, inappropriate care environments [9, 29-31]. The inability of traditional healthcare silos to meet the unique psychosocial and healthcare needs of this specific population is increasingly highlighted [32-34]. Place of treatment and delivery of cancer care, in terms of both disease and age-appropriate specialist settings is increasingly acknowledged as potentially significant to the outcomes for young people with cancer [35, 36].

To address these unique needs and deficit in outcomes' knowledge, in August 2005 the NICE *Improving Outcomes Guidance* recommended that all care for patients under 19 must be provided in age-appropriate facilities and those aged 19 and over should have 'unhindered access to age-appropriate facilities and support when needed' [1]. To accommodate this recommendation thirteen TYA PTCs were identified across England. Key components of the services of the TYA PTC encompass tumour site-specific expertise delivered in conjunction with meeting the broader psychosocial needs of young people to support successful navigation of critical life transitions. This is directed through the TYA multi-disciplinary team (MDT) [1]. But, despite national guidance supporting this approach to the delivery of cancer care for young people aged 15-24 years [1]. around half of young people continue to be treated in children's and adult cancer units with no or limited access to the TYA PTC, many receiving care in hospitals 'designated' by NHS commissioners to provide elements of specialist care that are available in a TYA PTC.

The aim of the BRIGHTLIGHT programme of research is to evaluate the benefit of specialist TYA cancer services for young people aged 13–24 years. The study has four key objectives specific to the cohort:

1. Relate the proportion of care young people received in a TYA PTC to: quality of life, satisfaction with care, clinical processes and clinical outcomes
2. Examine young people's experience of cancer care through a longitudinal descriptive survey
3. Compare social and educational milestones amongst young people receiving different levels of TYA cancer care
4. Determine the costs of specialist care to young people, their families and the NHS

Objectives

After 2nd review

The aim of this paper is to describe the complex recruitment process for establishing the BRIGHTLIGHT cohort, provide details of bespoke measures of levels of care and disease severity that were developed to inform the analysis of the evaluation, and to describe the baseline characteristics of the cohort.

STUDY DESIGN

The BRIGHTLIGHT cohort is a prospective longitudinal cohort study, obtaining data through a bespoke survey, administered through face-to-face interview, telephone interview and online, five times over three years: 5-7 months after diagnosis then at 12, 18, 24 and 36 months [37].

PATIENT AND PUBLIC INVOLVEMENT

The focus of this study was identified by young people as a priority area for research. BRIGHTLIGHT was preceded by a period of feasibility work where we worked with young as co-researchers to develop the research questions, outcome measures and study design [6, 9]. The study has a Young Advisory Panel who have worked with us since 2011, who have been integral in naming the study [5], study management [7, 8], identifying other areas for research [38] and dissemination [39].

SAMPLE AND SETTING

Participants

The BRIGHTLIGHT cohort included young people aged 13-24 years, newly diagnosed with cancer (ICD-10 codes C00-C97) in an English hospital and recruited within four-months of diagnosis. Eligibility criteria were as inclusive as possible so no restriction according to language or a sensory impairment that affected communication was applied. The only exclusion criteria were: young people receiving a custodial sentence; if the young person was not anticipated to be alive at the first point of data collection (6-months after diagnosis); recurrence of a previous cancer or they were not capable of completing a survey, e.g. sedated and in intensive care.

Recruitment

Young people present with a wide range of cancer diagnoses [11]. It was anticipated that to identify and recruit potentially eligible patients would be the biggest challenge because of: 1) low incidence 2) presenting to numerous points in healthcare system, due to age and multiple diagnostic subtypes; and 3) inconsistent referral pathways for tertiary care. The NICE guidance was issued in 2005 [1], and by 2010 only 40% of newly diagnosed young people were known to a TYA MDT based at a PTC [40]. Analysis of the national cancer datasets between 2010 and 2011 indicated that young people were being treated in an additional 133 hospitals across England. Thus, to capture the full cohort of young people we needed to open recruitment in as many hospitals as possible, have a mechanism to identify young people across the country and also have access to an extensive network of researchers to recruit and administer the study questionnaires.

After 2nd review

There were two mechanisms for identifying young people: first through the national Cancer Waiting Times (CWT) dataset, which has been reported in detail previously [41]. This is routinely collected NHS data used to monitor diagnostic and treatment targets; feasibility work suggested young people could be identified within three months of diagnosis [42]. However, when this method was applied nationally it was found to be neither timely nor accurate so a second mechanism was introduced: Principal Investigators were asked to liaise with the coordinators of all tumour-specific MDTs (except prostate cancer) so the person managing recruitment to the study could be informed of new diagnoses in young people aged 13-24 years. A third method to directly approach young people to invite them to participate was also introduced in the later stages of recruitment but did not significantly impact on accrual [43].

The second challenge was working with a very large number of hospitals, of which most were likely to identify a few eligible patients over the course of the study and who might present to one of several departments. BRIGHTLIGHT opened to recruitment in 109 hospitals, of whom 97 identified and recruited between 1-106 (median 5) young people per hospital, 12 not recruiting any participants. England has a national network of research personnel funded by the National Institute for Health Research (NIHR), tasked with facilitating recruitment into clinical studies [41]. The aim was to recruit 2,012 young people diagnosed between July 2012 and December 2013. Despite making multiple targeted amendments to the protocol and iteratively working with NIHR researchers and the TYA healthcare professional community to increase the proportion of patients who were offered study entry (supplemental file 1), recruitment was slower and lower than anticipated. In April 2014, an extension to recruitment until April 2015 was approved (young people diagnosed until December 2014, recruited within 4 months of diagnosis), and a lower target sample size was agreed (Figure 1).

Ethical approval and consent

The study was approved by London Bloomsbury NHS Research Ethics Committee (reference LO/11/1718). Approval by the Secretary of State under Regulation 5 of the Health Services (Control of Patient Information) Regulation 2002 was obtained from the Health Research Authority Confidentiality Advisory Group (reference ECC 8-05(d)/2011) to access the CWT dataset, Hospital Episode Statistic (HES) data and data from the National Cancer Registration and Analysis Service (NCRAS).

METHODS

Data were collected from three sources: young people, patient medical records, and central NHS and Public Health England (PHE) databases.

Data from young people

Patient-reported outcomes were collected from young people at five time points over three years: 4-7 months after diagnosis (wave 1), 12 months (wave 2), 18 months (wave 3), 2 years (wave 4) and a final data capture 3 years after diagnosis (wave 5). Data were collected using a study-specific questionnaire, the BRIGHTLIGHT Survey [37] (available under licence from https://xip.uclb.com/i/healthcare_tools/brightlight_wave1.html), which was administered as a face-to-face interview in young people's homes at wave 1. Subsequent

After 2nd review

waves were administered online or through telephone interviews. At wave 1, young people also completed study-specific health economics questionnaires, described below.

The BRIGHTLIGHT Survey

The BRIGHTLIGHT Survey is an investigator and young person-designed self-report questionnaire that was administered through computer-assisted personal, telephone or web interviewing or web by an independent research organisation. It was developed utilising patient-experience literature [44] and was underpinned by a conceptual framework to guide question content [9]. The BRIGHTLIGHT Survey contains five validated outcome measures and questions to reflect young people's experience of diagnosis and cancer care (Table 1) [37]. Completion of treatment occurs at different time points according to diagnosis. During the feasibility work young people emphasised that they did not want to be asked questions about cancer when treatment ended and therefore the computer administration of the BRIGHTLIGHT Survey had complex routing to ensure young people were only asked questions that were relevant to their current situation [37]. For example, questions related to pre-diagnosis and diagnostic experience were only asked at wave 1. The BRIGHTLIGHT survey also utilised 'pull through' options so that participants could reflect on responses given in previous waves before answering. For example, questions about employment/education goals were tailored so participants could be asked again at wave 5 to ascertain if goals had changed and if this was cancer-influenced.

Table 1: Summary of the content of the BRIGHTLIGHT Survey

Construct and questionnaire	Details
Quality of life – Pediatric Quality of Life Questionnaire (PedsQL™) [45]	Contains 23 items scored on a 5-point Likert scale. Four domains: physical, emotional, social and work/school functioning. Two summary scores (physical and psychosocial function) and a total score. Domain, summary and total scores on 0-100 scale, with 100 representing the best possible quality of life. Scores <69.7 indicate a high risk of impaired quality of life [46].
Health status – Euroqol- 5 Dimension 3 level (EQ-5D-3L) [47]	Comprises 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) scored on 3 levels (no, some, severe problems). The EQ visual analogue scale records self-reported health on a vertical scale ranging from 'best imaginable health state' to worst imaginable health state'. Scores 0-1 with 0 representing death and 1 perfect health (negative scores represent a health state worse than death).
Anxiety and depression – Hospital Anxiety and Depression Scale (HADS) [48]	A measure of depression and anxiety. Contains 14 items, scored on a four-grade scale (0 to 3). Summary scores for depression and anxiety (ranging from 0 to 21). Scores of 8-10 are defined as borderline and 11 and over are considered moderate/severe anxiety and depression [49].
Social support - Multi-dimensional Scale of Perceived Social Support (MSPSS) [50]	Scores for support by friends, family and significant others plus total support score. Contains 12 statements, rated on 7-point Likert scale.

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	Total support score is an average ranging from 1-7, sub-support scores range 4 – 28. Total scale score 1-2.9 are considered low support; a score of 3-5 is considered moderate support; and scores from 5.1-7 are considered high support.
Illness perception - The Brief Illness Perception Scale (BIPS) [51]	Measures the emotional and cognitive representations of illness. Contains eight* questions with fixed response scale specific for each question, e.g. not at all – extremely helpful. Each question represents a different dimension of illness perception: consequence, personal control, treatment control, timeline, identity, coherence, emotional representation, concern. Responses scored 1 – 10, the higher the score the greater perceived illness impact. No overall score and each question represents a single domain.
Cancer experience questions [37]	Comprises of 12 experience domains: pre-diagnosis experience, diagnostic experience, place of care, contact with healthcare professionals, treatment experience, fertility, involvement in clinical trials, adherence, communication and coordination of care, education, employment, wellbeing and relationships. Total of 238 questions with question specific responses describing experience

*Timeline statement not included

Health economics questionnaires

Cancer/treatment related costs incurred by young people and families were collected using a study-specific Cost of Care Questionnaire and Cost Record. These included questions regarding: travel (car parking, petrol and capital depreciation, public transport); time off work; medical equipment use; prescription and over the counter drug use; cost of accommodation incurred through hospitalisation; complementary and alternative medicine; and cost of family care for siblings. The Cost of Care Questionnaire was administered at wave 1 and required young people and their families to record costs incurred from the above items retrospectively since diagnosis. The Cost Record was given at waves 1 and 2, requesting the same information collected prospectively, on a weekly basis.

Data from medical records

Research teams who recruited young people completed an electronic Case Report Form (CRF) 12 months after diagnosis, which contained key variables relating to diagnosis, treatment, clinical process and outcome variables. This included postcode at the time of diagnosis, locations of care, details of diagnosis, MDT treatment planning and care, and outcomes at 12 months after diagnosis. The Index of Multiple Deprivation (IMD) is a measure of socioeconomic status [52] and was derived from the postcode at diagnosis, based on the population denominator of England. Clinical processes of care were defined as *documentation of*:

1. Histological diagnosis
2. Molecular diagnosis
3. Cancer stage or prognostic group
4. Initial treatment plan
5. Evidence of multidisciplinary communication

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6. Assessment by supportive care services, defined as documented contact with a Clinical Nurse Specialist plus one other member of the MDT (social worker, youth support coordinator, counsellor, psychologist, dietician, physiotherapist, occupational therapist)
7. Fertility discussion
8. Consideration for inclusion in a clinical trial

Data from national datasets

Data from NCRAS and HES were used to supplement and validate details of treatment received in the TYA PTC, to support a detailed health economic evaluation based on hospital attendance and healthcare received, and to cross check against the e-CRF. NCRAS data included date of diagnosis, tumour morphology, staging and treatment data; and HES data included dates for admitted patient care (APC), outpatient and accident and emergency attendance, plus receipt of chemotherapy and radiotherapy.

DEVELOPMENT OF BESPOKE METRICS

Defining levels of care

BRIGHTLIGHT aims to evaluate exposure to specialist TYA cancer services, defined as treatment in the TYA PTC. In recognition that patients may receive elements of care in more than one hospital, we proposed that care could be categorised by three levels according to the proportion of care received in a TYA PTC. To accurately allocate cohort participants to the appropriate level of care, analysis of HES data were used. In summary, PTC Trust codes were identified for 2012-2014 and applied to HES data so the proportion of days spent in a TYA PTC in the first 6 months and 12 months after diagnosis could be calculated (details provided in supplemental file 2).

Defining severity of illness

Advanced cancer is associated with poorer quality of life [53, 54]. We planned to compare quality of life of those treated in different care environments. To do so, we needed to consider ways to control for differences between patients which might influence this outcome and in particular, the severity of their cancer. However, this is difficult for TYA as they present with a heterogeneous array of malignancies [11]. While most cancers have staging criteria which differentiate between more or less extensive disease (typically groups 1-4 in ascending order of worsening survival), stage is not directly comparable between cancer types and a comparison based purely on staging would be meaningless due to the variation in outcomes between different cancers allocated to the same stage level. For example, stage 4 thyroid cancer is associated with a much higher chance of survival than say, stage 4 bowel cancer. Furthermore, survival alone is a good indicator of severity of illness as it takes no account of disease and treatment morbidity both for the short and long term. We therefore developed a bespoke 'severity' grading system to include symptom and treatment burden as well as predicted survival and burden of late effects. Each cancer type was graded as least, intermediate and most severe based on cancer-specific information thus allowing comparisons between groups of patients with multiple types of cancer (Table 2; detailed methodology is presented in supplemental file 3).

ANALYSIS

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The number of young people at each stage of the project were described using a flow diagram, including the numbers eligible, consenting to be involved, and followed up at each survey point. Reasons for non-participation at each stage were summarised. Potentially eligible patients who did not participate in the cohort study were compared against those who consented with regard to age, gender, ethnicity, location (based on the network linked to each PTC) and diagnosis. Data in both groups were summarised as means with standard deviations (sd), medians with interquartile ranges (IQR) or frequency and percentage (%), as appropriate and comparisons made using standard Chi squared and t-tests Since sample sizes for these comparisons were very large, statistical significance is defined as P<0.001. Survival from diagnosis was summarised using Kaplan Meier plots and the cohort and non-cohort groups compared using Cox regression to adjust for age, gender, ethnicity, location and type of cancer. Patient reported outcomes collected in the first wave were scored according to published guidance for each of the validated measures. The characteristics of the cohort were summarised using means/medians (sd/IQR) or frequency (%) as appropriate.

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Table 2: BRIGHTLIGHT Severity of Illness Index (see supplemental file 3)

Cancer type [11]	**Least severe**	**Intermediate severity**	**Most severe**
Germ cell tumours	Stages 1-3; Stage unknown	Stage 4 (stage 1S=stage 4)	
Leukaemias	CML	ALL; Other and unspecified	AML
Non-Hodgkin lymphoma and non-specified lymphoma	Over 16yrs, protocol unknown Stage 1-2	Over 16s, protocol unknown; Stage 3-4; Any paediatric-type protocol; All unknown	Burkitts (ICD10 C83.7, morphology code 9687/3)
Hodgkin lymphoma	All stages		
Central nervous system tumours	Pituitary adenomas (D35.2); Sub-ependymal giant cell astrocytoma (C43.2)	Other completely resected WHO grade I tumours for which surgery is the only treatment needed - except craniopharyngiomas	Craniopharyngiomas; incompletely resected or unresectable grade I tumours; all grade II-IV tumours, any needing radiotherapy or chemotherapy. This includes ependymomas, medulloblastomas and intracranial GCTs
Bone tumours	Surgery only (low grade, periosteal, parosteal)		All other
Soft tissue sarcoma	Stages 1-2	Stage 3; Unknown	Stage 4
Rhabdomyosarcoma	Low risk EpSSG A-D[1]		All others; Unknown
Melanoma	Stages 1-2 (except 2c)	Stage 2c; Stage 3 (except 3c); Stage unknown	Stage 3c; Stage 4
Carcinoma	All thyroid; All Stage 1; Cervix stage unknown	Stages 2-3; All nasopharyngeal; Stage unknown (except cervix)	Stage 4
Miscellaneous and unspecified		All	

[1] EpSSG: European Paediatric Soft Tissue Sarcoma Study Group

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RESULTS

A total of 1,126 young people were recruited for whom valid consent was available from 1,114 (Figure 2). Recruiting hospitals were required to keep a screening log, which was returned to the BRIGHTLIGHT team by 95 (87%) hospitals when recruitment ended. Of the 2,900 young people who had been screened, 429 (15%) were reported as not being eligible and 1,877 (65%) were eligible to participate. No details were provided for the remaining 594 (20%). Only 426 (23%) of those eligible had refused to participate, which was lower than the 35% we had anticipated and accounted for [8]. Of the 15% recorded as being ineligible, just over half (225, 52%) had either no reason recorded or appeared to have been deemed to be ineligible incorrectly.

Data were obtained from NCRAS for young people diagnosed in the same time period, who were potentially eligible, i.e., alive 6-months after diagnosis and place of residence was not linked to a prison postcode. A total of 5,953 young people were diagnosed with cancer between July 2012 and December 2014, of whom 5,835 (98%) were potentially eligible to participate[1]; 1,114 (19%) appeared in the BRIGHTLIGHT Cohort.

Clinical and NHS data were available for all 1,114 young people. Of these, 830 (75%) completed the wave 1 survey (Figure 2). In total, 163 (20%) participated once, 186 (22%) twice, 195 (24%) completed three, 173 (21%) completed four and 113 (14%) took part in every wave.

Non-participants were similar in age and ethnicity to those in the BRIGHTLIGHT cohort but there were differences in gender (a lower proportion of males in non-participants) and inclusion by tumour type (a greater proportion of young people with leukaemia and lymphoma, germ cell tumours and bone tumours compared to non-participants but lower representation of brain tumours, skin cancers and carcinomas) (Table 3).

Table 3: Comparison of characteristics of participants and non-participants

		N	BRIGHTLIGHT Cohort	N	Non-Participants	P-values[3]
Age at Diagnosis (years)	Mean (SD) Median (IQR)	1114	20.13 (3.28) 20.64 (17.58, 22.95)	4721	19.94 (3.33) 21 (17, 23)	0.08
Gender	Male Female	1114	618 (55%) 496 (45%)	4721	2213 (47%) 2508 (53%)	<0.0001
Ethnicity	White Asian Black Chinese Mixed Other	1085	936 (86%) 82 (8%) 22 (2%) 4 (<1%) 26 (2%) 15 (1%)	4316	3643 (84%) 288 (7%) 156 (4%) 34 (<1%) 74 (2%) 121 (3%)	0.002
Type of cancer[1]	Leukaemia Lymphoma CNS	1114	145 (13%) 350 (31%) 46 (4%)	4721	300 (6%) 781 (17%) 735 (16%)	<0.0001

[1] 109 young people died within 6-months of diagnosis so were assumed to be too sick to be approached and nine were in prison.

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	Bone		102 (9%)		177 (4%)	
	Sarcomas		78 (7%)		207 (4%)	
	Germ cell		212 (19%)		504 (11%)	
	Skin		45 (4%)		709 (15%)	
	Carcinoma (not skin)		125 (11%)		1210 (26%)	
	Miscellaneous specified		9 (<1%)		55 (1%)	
	Unspecified malignant		2 (<1%)		43 (1%)	
Geographical location[2]	Birmingham	1114	155 (14%)	4618	459 (10%)	<0.0001
	Bristol		116 (10%)		351 (8%)	
	Cambridge		23 (2%)		276 (6%)	
	Manchester		103 (9%)		391 (8%)	
	Merseyside		42 (4%)		239 (5%)	
	East Midlands		135 (12%)		278 (6%)	
	Leeds		106 (10%)		254 (6%)	
	Newcastle		59 (5%)		305 (7%)	
	Oxford		19 (2%)		249 (5%)	
	London (south)		77 (7%)		668 (14%)	
	Sheffield		37 (3%)		174 (4%)	
	Southampton		83 (8%)		221 (5%)	
	London (north)		159 (14%)		753 (16%)	

CNS: central nervous system; SD: standard deviation; IQR: interquartile range

[1] Based on the Birch classification [11]

[2] Hospitals mapped to the multidisciplinary team at the Teenage and Young Adult Principal Treatment Centre they were linked to

[3] P-values from Chi squared tests and t-tests as appropriate.

Of the 1,114 young people in the BRIGHTLIGHT cohort, 618 (55%) were male, mean age at diagnosis was 20.13 years (SD 3.28) and 936 (86%) identified themselves as white. Lymphoma was the most common cancer type (n=350; 31%), followed by germ cell tumours (n=212; 19%) and leukaemia (n=145; 13%) (Table 3). Table 4 details the sociodemographic and clinical characteristics of the BRIGHTLIGHT cohort. There was an even distribution across socioeconomic groups. Most were single (n=606; 84%) and employed or in education (n=531; 64%). Systemic anti-cancer therapy was the most common form of treatment, used for 880 (79%). Thirty (3%) young people received no treatment, just active monitoring. The clinical processes that were most frequently documented in the clinical records were MDT communication (n=1037; 97%), cancer stage or prognostic group (n=1015; 94%), histology (n=974; 91%) and initial treatment plan (n=974; 91%). One hundred and sixty seven (20%) young people reported having a pre-diagnosis long-term condition.

Table 4: Socio demographic and clinical characteristics of the BRIGHTLIGHT Cohort

Characteristic		Number	%
Socioeconomic status (IMD quintile) (N=1088)	1 – most deprived	250	23
	2	194	18
	3	209	19
	4	230	21
	5 – least deprived	205	19
Marital Status (wave 1; N=725)	Married/civil partnership	26	4
	Cohabiting	93	13
	Single/divorced	606	84
Current status	Working full/part time	257	31

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(at wave 1; N=830)	In education	274	33
	Other work (apprentice/intern/voluntary)	17	2
	Unemployed	31	4
	Long term sick	126	15
	Not seeking work	125	15
Length of inpatient stay over 12 months (N=1070) days	Median (IQR)	25	9 to 74
Treatment (N=1114)[2]	Systemic anti-cancer therapy	880	79
	Radiotherapy	324	29
	Surgery	551	50
	Active monitoring	30	3
	Transplant (stem cell or bone marrow)	28	3
Severity of illness (N=1114)	Least	611	55
	Intermediate	254	23
	Most	249	22
Clinical processes of Care (documentation available in clinical records)	Histological diagnosis (n=1072)	974	91
	Molecular diagnosis (n=737)[3]	258	35
	Cancer stage or prognostic group (n=1078)	1015	94
	Initial treatment plan (n=1071)	974	91
	MDT communication (n=1074)	1037	97
	Assessment by supportive care services (n=1057)	563	53
	Fertility being discussed (n=1063)	693	65
	Consideration into a clinical trial (n=1057)	676	64

CNS: central nervous system; IMD: Index of Multiple deprivation; IQR: interquartile range

[1]Based on period of 12 months from diagnosis. Missing for 70 participants: 26 had no days in hospital after diagnosis (inpatient stay was before diagnosis date) and data were missing for 44

[2] N greater than 1114 reflects multiple treatment modalities for some diagnoses

[3] Where relevant, indicated as not relevant in 320

A total of 124 (11%) young people in the BRIGHTLIGHT cohort died before 31st December 2016. Results from Cox regression indicate that a survival benefit for non-BRIGHTLIGHT patients was maintained even after adjustment for age, gender, ethnicity and type of cancer; the risk of death was 34% higher for those in the BRIGHTLIGHT cohort compared with those not in the cohort. (Figure 3; hazard ratio estimate 1.34 (95% confidence intervals 1.09-1.68), p=0.01; table 5). There was no evidence that survival of cohort participants compared with non-participants differed by cancer type (P-value for interaction P=0.12).

Table 5: Comparison of survival between participants in the Cohort and non-participants[1]

Estimated cumulative survival probabilities by year from diagnosis (95% CI)		
	Non-participants	BRIGHTLIGHT cohort
1 year	0.98 (0.97, 0.98)	0.98 (0.97, 0.99)
2 years	0.95 (0.94, 0.96)	0.92 (0.91, 0.94)
3 years	0.93 (0.92, 0.94)	0.89 (0.87, 0.91)
4 years	0.92 (0.91, 0.93)	0.88 (0.85, 0.90)

CI: confidence intervals

Log rank test P value <0.0001

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[1]Non-participants were young people diagnosed in the same time frame as the BRIGHTLIGHT cohort identified by the National Cancer Registration and Analysis Service (NCRAS), who were not part of BRIGHTLIGHT

A summary of patient-reported outcomes recorded at wave 1 are presented in Table 6. Mean total quality of life, physical and emotional domain scores were <69.7 indicating that, on average, young people had some impairment to quality of life shortly after diagnosis [46]. This is particularly notable in terms of physical scores where the average was significantly below the threshold, by more than 10 points, for a clinically important difference [55, 56]. Forty percent of young people could be classified as 'cases' for anxiety and 22% for depression (borderline-severe) [49]. Young people reported high levels of support from friends (Multi-dimensional Scale of Perceived Social Support cut off >5) and moderate support from family and significant others (score 3-5) [50]. The Brief Illness Perception Scale results indicate that young people felt cancer had a moderate effect on their life but they perceived that treatment was extremely helpful. They perceived themselves as having experienced a moderate number of symptoms and believed they had a good understanding of their cancer. The majority rated their satisfaction with care as being excellent/good (n=777; 94%). Those aged 19-24 years seemed to have better physical and psychosocial quality of life compared to those aged 13-18 years at diagnosis. This older age group also reported more anxiety, lower social support, better perceived personal control but lower perceived emotional representation and concerns. According to diagnosis, young people with a solid tumour had better physical scores, perceptions of consequences and identity but less support from friends than those with a blood cancer. Finally, there was a noticeable trend for better total quality of life, physical and psychosocial scores for those with less severe disease and worse emotional score for the intermediate severity group. Young people with less severe disease had better perceived consequences and identify but satisfaction with care was highest in those with the most severe disease.

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Table 6: Summary of the wave 1 patient-reported outcomes

			Age		Diagnosis		Severity of illness		
Characteristic	**N**	**All patients N=830**	**13-18yrs N=302**	**19-24yrs N=528**	**Haematology N=373**	**Oncology N=457**	**Least N=461**	**Intermediate N=194**	**Most N=175**
PedsQL - mean (SD)									
Total score	829	66.20 (19.79)	64.14 (18.53)	67.39 (20.40)	64.59 (18.28)	67.52 (20.86)	70.67 (18.86)	61.55 (19.77)	59.57 (19.25)
Physical summary score	828	59.45 (27.72)	54.67 (26.75)	62.20 (27.91)	56.96 (25.04)	61.47 (29.58)	67.65 (25.49)	52.67 (26.63)	45.33 (26.95)
Psychosocial summary score		80.38 (18.45)	77.88 (18.27)	81.82 (18.42)	79.37 (18.49)	81.21 (18.41)	84.15 (16.75)	75.90 (19.82)	75.43 (18.98)
Emotional summary score		67.64 (22.76)	70.94 (21.83)	65.75 (23.07)	67.75 (21.68)	67.55 (23.62)	68.05 (23.09)	64.92 (23.15)	69.57 (21.21)
EQ-5D – mean (SD)	830	0.76 (0.24)	0.75 (0.23)	0.77 (0.24)	0.77 (0.22)	0.76 (0.25)	0.81 (0.21)	0.71 (0.26)	0.71 (0.24)
Total score									
- **median (IQR)**		0.80 (0.69-1)	0.80 (0.62-1)	0.81 (0.69-1)	0.80 (0.69-1)	0.80 (0.66-1)	0.85 (0.73-1)	0.73 (0.62-1)	0.75 (0.59-0.88)
HADS – mean (SD)[1]	830								
Anxiety score		6.89 (4.39)	6.14 (4.12)	7.32 (4.49)	6.79 (4.36)	6.98 (4.43)	7.23 (4.55)	7.01 (4.44)	6.14 (3.83)
- Borderline n (%)		160 (19%)	51 (17%)	109 (21%)	75 (20%)	85 (19%)	82 (18%)	44 (23%)	34 (19%)
- Moderate/severe n (%)		172 (21%)	48 (16%)	124 (23%)	70 (19%)	102 (22%)	106 (23%)	40 (21%)	26 (15%)
Depression score		4.62 (3.68)	4.45 (3.38)	4.71 (3.84)	4.84 (3.57)	4.43 (3.76)	4.31 (3.65)	5.16 (3.79)	4.81 (3.57)
- Borderline n (%)		120 (15%)	40 (13%)	80 (15%)	48 (13%)	72 (16%)	48 (10%)	40 (21%)	32 (18%)
- Moderate/severe n (%)		55 (7%)	16 (5%)	39 (7%)	26 (7%)	29 (6%)	32 (7%)	14 (7%)	9 (5%)
MSPSS – median (IQR)									
Total support	820	1.50 (1.08-2.25)	1.58 (1.17-2.33)	1.50 (1-2.08)	1.58 (1.08-2.25)	1.42 (1.08-2.17)	1.50 (1.08-2.25)	1.58 (1-2.25)	1.50 (1.17-2.08)
Support - friends	827	7 (4-11)	7 (4-12)	6 (4-10)	7 (4-11)	6 (4-10)	7 (4-10)	7 (4-12)	7 (4-10)
Support - family	827	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	5 (4-8)	4 (4-7)
Support – significant others	823	4 (4-8)	5 (4-9)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-8)	4 (4-9)	4 (4-7)
BIPS – median (IQR)	830								
Consequences		7 (4-8)	7 (5-8)	7 (4-8)	7 (5-8)	6 (4-8)	6 (4-8)	7 (5-8)	7 (6-9)
Personal control		6 (4-8)	6 (5-8)	5 (3-8)	6 (4-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Treatment control		10 (9-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (8-10)	10 (9-10)	10 (9-10)	10 (8-10)
Identity		5 (3-7)	6 (3-8)	5 (3-7)	6 (4-7)	5 (2-7)	5 (3-7)	6 (3-8)	6 (4-8)
Coherence		8 (7-10)	9 (7-0)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	8 (7-10)	9 (7-10)
Emotional representation		6 (4-8)	5 (3-7)	7 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (4-8)	6 (3-8)
Concern		6 (3-8)	5 (3-7)	7 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)	6 (4-8)	6 (3-8)
Satisfaction with care – n (%)	820								
Excellent/good		777 (95%)	284 (95%)	493 (95%)	358 (96%)	419 (94%)	433 (95%)	173 (91%)	171 (99%)

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Fair/poor/very poor		43 (5%)	16 (5%)	27 (5%)	15 (4%)	28 (6%)	23 (5%)	18 (9%)	2 (1%)

BIPS: Brief Illness Perception Scale; EQ-5D: Euroqol 5-Dimension; HADS: Hospital Anxiety and Depression Scale; IRQ: interquartile range; MSPSS: Multi-dimensional Scale of Perceived Social Support; PedsQL: Pediatric Quality of Life Questionnaire;SD: standard deviation

[1]Borderline = 8-10, moderate/severe = >11 [49]

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DISCUSSION

The BRIGHTLIGHT cohort is the first national, prospectively recruited cohort of teenagers and young adults with cancer. We are able to examine in detail the complexity associated with place of care, experience and outcome. This is made possible through the use of linked data from multiple sources so unlike other cohorts which rely solely on patient-reported outcomes [34, 54] or clinical data [32], a more comprehensive evaluation can be derived. Using national mandatory NHS datasets we have been able to calculate a more robust measure of time spent in specialist TYA care. Other data sources, such as secondary analysis of the National Cancer Patient Experience data is based on TYA PTC code at the time of participation [57], as such this reflects a single point in time and does not reflect experiences and outcomes for those who have exposure to both specialist and non-specialist care. Measuring exposure to a TYA PTC through analysis of HES data has enabled a more objective exposure variable to be developed. Similarly, defining severity of cancer through prognosis for survival alone does not reflect the symptom/treatment burden of disease and the impact this has on quality of life during treatment and recovery. Systematically defining prognosis alongside symptom and treatment burden, provides a more nuanced measure and is a better reflection of the severity of illness.

Selecting the study design to evaluate TYA cancer services across England was challenging as services were already in place and, in some regions of the country, long-established. There was also wide variation in implementing the NICE Guidance [1] according to local need and pre-existing resources, resulting in services at PTCs not being identical. The decision to establish a cohort was made on the basis that it is suited for investigating rare exposures, allows examination of multiple outcomes for the defined exposure (to specialist care), and would enable us to gather data regarding sequence of events, with the potential to assess causality. The main limitation of the cohort is we only recruited a fifth of the population who were eligible to participate. Variation in diagnosis and severity between those in the cohort receiving different level of PTC care reduces the potential to assess causality.

Cohort studies are acknowledged to be challenging to establish and maintain, especially in rare conditions due to the requirement for large numbers of subjects, potential for selection bias and the challenges associated with subject retention [58-61]. We anticipated that participation might favour those who were less unwell or had a better prognosis. The inclusion of significant numbers with tumours associated with poorer prognosis such as bone tumours and the inferior survival of the cohort go against this. One of the aims of the BRIGHTLIGHT was to evaluate socioeconomic variation in access to specialist care. A comparison of IMD quintile between those who were and were not recruited who have enabled us to assess whether there was bias in recruitment according to difference socioeconomic groups; however, these data were not available but warrant exploration in the future. Our experience of recruitment points to the value of maintaining accurate screening logs and seeking mechanisms to complement the intelligence from local teams about change of status of participants such as death or change of address.

Our experience highlights the value of patient and public participation in research. We have described earlier in the paper the involvement young people had from study inception to

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dissemination. In total more than 1,200 young people have been involved in BRIGHTLIGHT as part of the research process almost the same number as those recruited. We believe this has positively influenced the rates of participation, ways in which young people were approached and methods of data collection, and doubled the retention rate at Wave 3 [7].

This population is known to have lower involvement in clinical trials in comparison to children and older adults [22, 62], yet there have been no targeted interventions developed to improve recruitment [63]. We have reported that to optimise recruitment to clinical trials, what we have identified as 'the 5'A's' need to be addressed, namely availability, accessibility, awareness, appropriateness, and acceptability [62]. We have identified factors that young people feel are acceptable for accessing research [8] and for continuing their involvement in a study [7]. We have also identified that the networked structures for facilitating recruitment into cancer research in England may not be optimal for the recruitment of young people [41]. The impact of not having an optimal research network was made apparent through BRIGHTLIGHT, as it was the first national study in this population. Ways to overcome this challenge are currently being explored by the NIHR.

A potential limitation of the BRIGHTLIGHT cohort study is the outcome measures that were selected to be included in the survey. Traditionally outcome measures are developed for children less than 18 years or adults older than 18. Our population crossed both age groups so there were limited measures validated for use in this population. Our measure of quality of life, the PedsQL, has been validated for use in adolescence and adulthood [45] and has been used often in TYA cancer studies [34, 64-67]. The other measures, outlined in Table 1, had no formal psychometric testing specifically in a TYA cancer population. However, these have been used extensively in studies in young people with and without cancer [68-74] so we are confident the results reflect a consistent measure of each construct, but warrants further exploration of the data in the future.

FUTURE PLANS

The BRIGHTLIGHT cohort was originally designed to evaluate short-term outcomes, from early after diagnosis to three years after diagnosis, over five time points. Data collection for wave 5 ended in February 2018, with results for the four key objectives anticipated to be available by the end of 2018. As noted earlier, the study has generated a large quantity of data and with the recent completion of a James Lind Alliance Priority Setting Partnership exercise for TYA exercise (http://www.ncri.org.uk/ncri-blog/top-10-research-priorities-for-teenage-and-young-adult-cancer-identified/), there is the opportunity to address some of the unanswered questions with the BRIGHTLIGHT cohort. This opportunity has already been realised to contribute evidence to improvements in early diagnosis [19]. In line with NIHR guidance, patient-reported outcome data from the cohort will be made available to external researchers on acceptance of the final report in the NIHR Journal Library. Details of how to apply will be made available on the website (www.brightlightstudy.com).

The philosophy of specialist TYA cancer care is to provide optimal cancer treatment alongside the developmentally-sensitive care that enables young people to achieve their life goals (e.g. education, employment, relationships) during treatment and beyond. BRIGHTLIGHT will evaluate this in the short-term but longer-term follow-up may be valuable

to explore whether the model of care delivery influences these outcomes later in life. We are now planning a 10-year follow-up study to assess the long-term impacts. We also acknowledge that similar to other studies quantifying care using NHS data [57, 75], the measure of specialist care may lack discrimination, not least because it assumes that all TYA PTCs and other places of care are equal. Additional to the cohort, a case study was conducted to understand the culture of TYA cancer care [3]. There is the potential to synthesise the qualitative findings from the case study with the quantitative data from the cohort to develop a more detailed and sensitive metric to define specialist TYA cancer care. Ultimately, the data generated by the cohort and BRIGHTLIGHT will provide new information on cancer in young people and determine if access to a PTC adds value. The relationships between specialist care and outcomes have previously been unclear. Findings will inform intervention and policy efforts to improve outcomes for young people with cancer.

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RMT, LAF, JB, DS, SM, RF, LH, MM, FG, RR, JSW were involved in developing the protocol. RMT coordinated the running of the study and was responsible for data acquisition. JB, JGA, RMT, LAF, SM, RF, DS, JSW contributed to the analysis. RMT, LAF, JB and JSW drafted the manuscript. All authors critically revised and approved the final manuscript.

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None declared.

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Data sharing statement:
Further details of the BRIGHTLIGHT programme of work is available through the study website (www.brightlightstudy.com). Data that are not held under licence with Public Health England or NHS Digital will be available from late 2018 when the primary analysis is complete. We welcome collaboration, for general data sharing enquiries please contact RMT (rtaylor13@nhs.net).

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Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures

i. Open to most Trusts agreeing to participate (n=77); posters to advertise BRIGHTLIGHT distributed to all Trusts
ii. Information to all newly diagnosed young people distributed in CLIC Sargent information packs; top recruiters reported in the TYAC weekly bulletin (the professional organisation in the UK supporting healthcare professionals with adolescents and young adults with cancer)
iii. Healthcare professional information leaflets sent to all Trusts (hard copy and electronic for local distribution)
iv. Director/Assistant Directors of the National Cancer Research Network emailed all the Cancer Network Managers directing them to make recruitment to BRIGHTLIGHT a priority; approved amendment to allow consent to be taken the same time a giving the information sheet
v. Review of screening logs and site specific feedback presentations sent to each Principal Treatment Centre (PTC)
vi. Open to recruitment in all 13 PTCs
vii. Approval to use social media to recruit young people; open in all 109 Trusts agreeing to open to recruitment
viii. Attendance at a Teenage Cancer Trust Lead Nurse event to highlight recruitment issues and gain support
ix. Emails sent by universities (communication teams or student unions) to current students with a link to the website to capture young people continuing with education after diagnosis; training for Youth Support Coordinators to be able to recruit young people
x. Attend a CLIC Sargent Social Worker event to promote the study and gain support to take a recruitment role
xi. Information on the BRIGHTLIGHT website in video format
xii. Recruitment method based on the National Cancer Patient Experience Survey implemented

Figure 2: A summary of participation at each wave of data collection

* Drop outs between waves due to death, permanent opt-out or wave opt out. Wave opt-outs prior to being issued were not permanent opt-outs; participants could opt-out of a single wave but participate in subsequent waves; these cases were not removed from the cohort permanently

Figure 3: Comparison of survival between participants in the Cohort and non-participants[1]

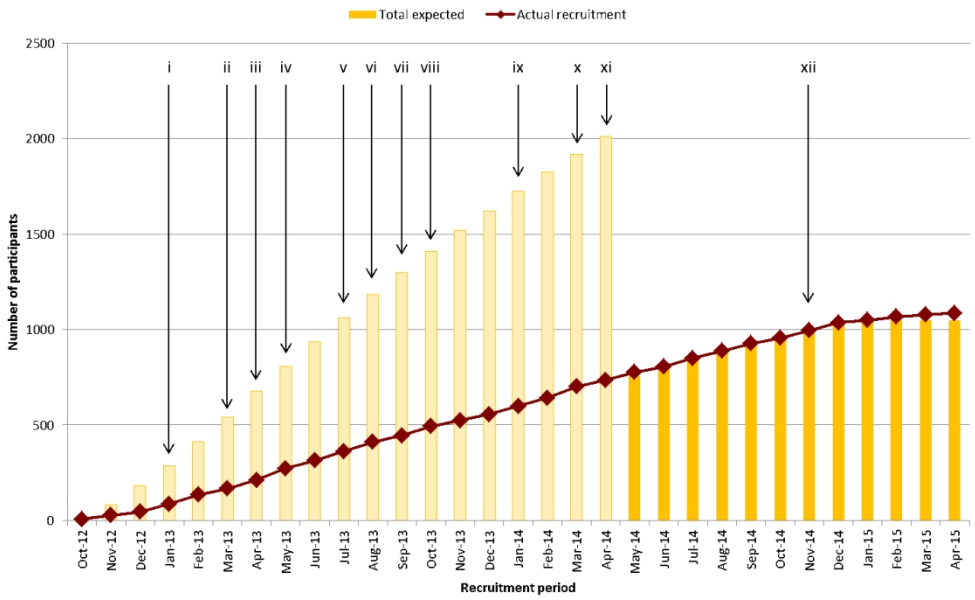


Figure 1: Summary of actions undertaken to improve recruitment and impact on accrual figures

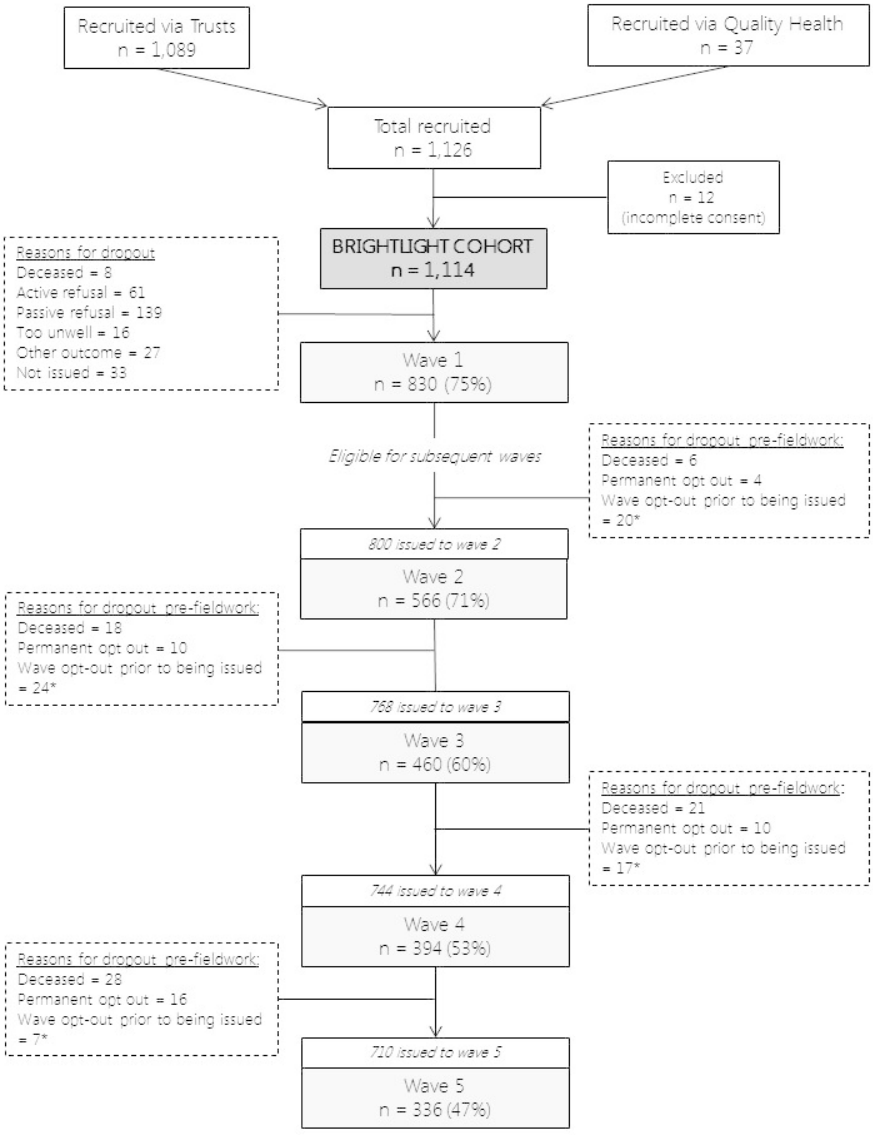


Figure 2: A summary of participation at each wave of data collection

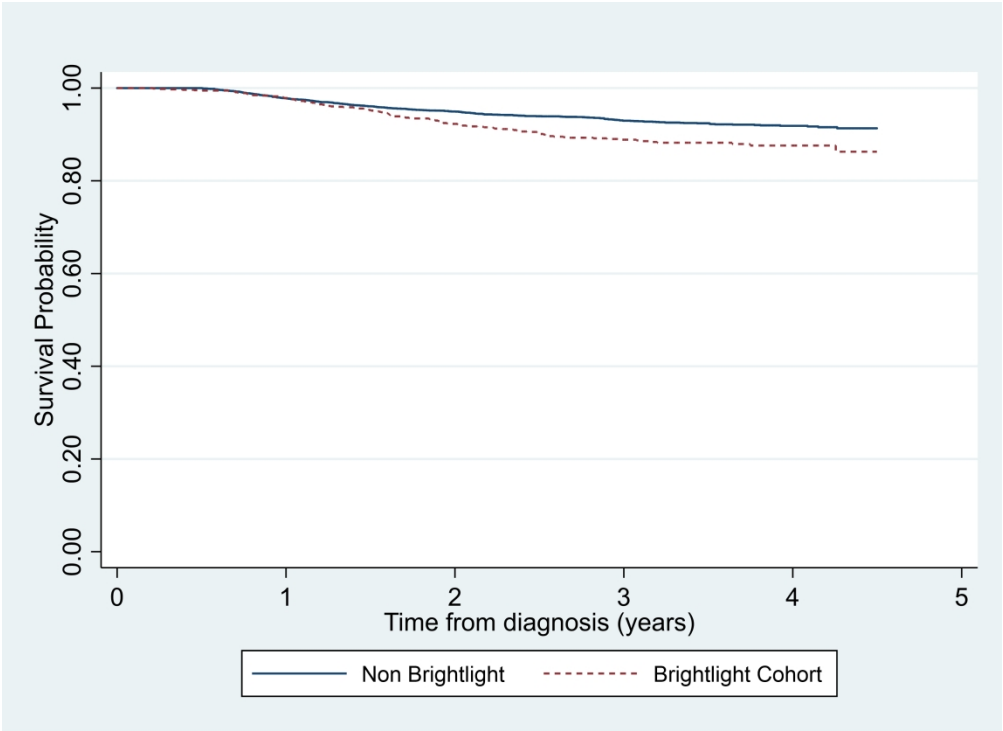


Figure 3: Comparison of survival between participants in the Cohort and non-participants

BRIGHTLIGHT Cohort profile – supplementary file 1

Supplementary File 1 Detailed results of actions implemented to improve recruitment to the cohort

Table A: Possible challenges reported by healthcare professionals before recruitment began and strategies identified to overcome them

	Challenges	**Strategies proposed to overcome challenges**
Identifying young people	Missing eligible young people if transferred to regional specialist centres Recruiting across a range of hospital sites Recruiting across multiple tumour types Engaging consultants: one concern was they would not think the older TYAs were eligible, a perception being that it was a 'teenager' study	Use the TYA MDT meetings to identify young people Co-ordination by a key person such as the Lead Nurse, cancer network head, or MDT lead to ensure details of eligible TYAs are passed to the recruiters Collaborative working with other centres to ensure all young people are approached, but not on multiple times
Approaching/consenting young people	Concerns about 'getting past' protective and upset parents Timing of consent, particularly if the patient is undergoing chemotherapy and was likely to be feeling very unwell Lack of experience in working with 'children' Being seen or felt to 'pressurise' potentially 'vulnerable and fragile' young people to take part Getting treating consultant approval to approach young people	Encouraging the initial approach to be a conversation, and not be immediately about persuading young people to take part Work with paediatric nurses to help with recruiting younger TYA Undertake paediatric consent training Wait for a sufficient length of time after diagnosis – maybe two months – before introducing the study, to allow the young person to become accustomed to the emotional and practical impact of the diagnosis

TYA: Teenage and young adult; MDT: multi-disciplinary team

BRIGHTLIGHT Cohort profile – supplementary file 1

Table B: Suggestions from healthcare professionals for keeping young people engaged throughout the study

Suggestion to keep young people engaged	**Action for implementation by BRIGHTLIGHT**
Get the consent process absolutely right: clear, accurate information about the survey, as buy-in from young people will increase the chances they will continue to participate	Information developed with young people, site initiation with recruiters to ensure they knew about the study and could relay information to young people in the best way
Provide TYA-friendly formats: e.g., ensure the survey could be completed on an iPad or iPhone as well as on a home computer	The survey was administered face-to-face at the first time point; subsequently it could be completed online on any platform
Use the internet: communicate via social networks like Facebook and Twitter	An open Facebook account was prohibited by the sponsor Trust but a Twitter account was opened
Ensure language used is aimed at empowering young people	All information was reviewed by the YAP[1] and had a reading ease of >70%
Consider incentives: e.g., a medal-based reward system – for each year young people remain in the study they move up the medals from Bronze (Year 1) to Silver (Year 2) and Gold (Year 3) and get a correspondingly increasingly valuable reward each time.	The YAP suggested a reward system using wrist bands with a different colour for each wave of participation
Inform participating young people on why the study matters and why their continuing involvement is important	A website was developed to keep young people updated about the programme www.brightlightstudy.com
Maintain contact throughout	Newsletters
Disseminate progress and results so they can see the wider scale and impact of the survey, that is making a difference	Content of newsletters related to results as far as was possible
Keep parents on board perhaps with targeted communications	Newsletters sent to all the email addresses provided
Distribute posters and flyers to treatment centres	Posters and flyers provided

YAP: Young Advisory Panel; TYA: teenage and young adult

[1]YAP are the BRIGHTLIGHT patient user group

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C: Suggestions for how the BRIGHTLIGHT Team might facilitate recruitment and actions taken to address these

Suggested change	Action by the BRIGHTLIGHT Team
1. Study information for health professionals	An information booklet was developed giving a brief summary of the study. This was sent electronically and as hard copies to all participating Trusts. Regular newsletters were developed and circulated online and as hard copies. Recruitment figures were circulated in a weekly Bulletin by TYAC to their members and were also Tweeted by the BRIGHTLIGHT team (@bR1GhTLiGhT)
2. Make the participant information sheets as short as possible	A summary booklet had been produced by Ipsos MORI[1] to send as a reminder about the study by their interviewers. An ethics amendment was made in July 2013 to allow this to be used in conjunction with the lengthy information sheet at the time of consent. Video versions of the information sheet were made available on the website (www.http://www.brightlightstudy.com/user-involvement/)
3. Investigate any variation in recruitment rates between sites	Screening logs were requested and analysed to identify reasons for suboptimal recruitment, which was fed back to each Trust with guidance on how to overcome recruitment issues.
4. Reduced interval between giving information and getting consent[2]	An amendment was approved by the Ethics Committee to allow consent to be taken within the same 24-hour period as information was given.
5. Provide BRIGHTLIGHT advertising materials	Posters, flyers and postcards had been available since the beginning of the study. These were distributed not only by the BRIGHTLIGHT Team but also by CLIC Sargent and Teenage Cancer Trust.
6. Keep sending the NWCIS notification[3]	There was a temporary pause in the CWT data being sent due to organisational change of NWCIS to Public Health England.
7. Extend the window of recruitment for wave 1	This was relaxed at the end of 2012 so young people could be recruited at any time in the first four months after diagnosis. We were unable to extend recruitment beyond this period because we wanted data to be collected within a specific time window. Young people were not able to enter the study at later time points because subsequent questions were informed by responses in the first survey.

BRIGHTLIGHT Cohort profile – supplementary file 1

Table C. *cont.*

Suggested change	Action by the BRIGHTLIGHT Team
8. Reduce the number of times young people need to participate (total study participation involved 5 time points in 3 years)	The sample size calculation was based on participation at three time points (as specified in the protocol) because we were aware young people might opt in and out of participation depending on their current life commitments. We developed top tips for recruiting Trusts, including information about participation. The top tips were prominent on the website, were sent as an information leaflet, and included in the newsletter.
9. Enable information sheets to be posted to young people	An ethics amendment was approved to enable information sheets and consent forms to be posted and/or returned through the mail.
10. Make presentations at local network and Trust meetings	Members of the BRIGHTLIGHT team presented recruitment updates at every available national meeting. Trusts were also informed that the team would come to any local meetings on request. Site specific slides to present at MDTs were provided to all PTCs.
11. First survey to be online or telephone rather than face-2-face	This request could not be accommodated. A single mode of administration had been developed for the first survey.[4]

CWT: Cancer Wait Time database; MDT: multi-disciplinary team; NWCIS: North West Cancer Intelligence Service (after the move to Public Health England became known as the North West Knowledge Intelligence Team). PTC: Principal Treatment Centre; TYAC: Teenagers and Young Adults with Cancer (the organisation representing healthcare professionals working in this area).

[1] Ipsos MORI were the commercial company administering the BRIGHTLIGHT Survey; [2] Ethics guidance in the United Kingdom recommends a minimum of 24 hour between providing information and gaining consent to give participants time to process information; [3] NWCIS sent a monthly email to a dedicated person in each recruiting trust with a list of potentially eligible patients identified through the Cancer Waits dataset as newly starting treatment; [4]Subsequent waves had a choice of online or telephone interviewer administered survey; the online option has only been selected by a minority of young people

BRIGHTLIGHT Cohort profile – supplemental file 2

Supplemental file 2: Method for calculating the TYA Cancer Specialism Scale (TYA CSS) to assign level of care

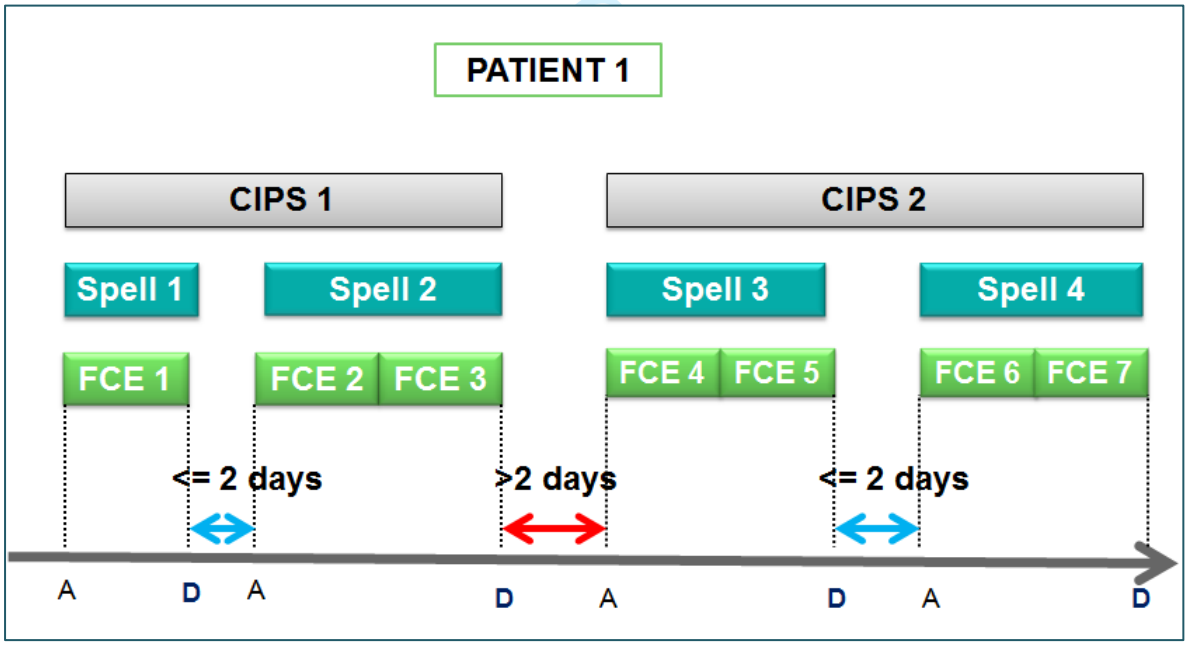
The TYA CSS is derived from admitted patient care data using linked Hospital Episode Statistic (HES) data. HES data from 2011/12 to 2016/17 were obtained from NHS Digital and linked to patients from the BRIGHTLIGHT cohort using the following identifiers: NHS Number, sex and postcode. The method for calculating the TYA CSS is adapted from an approach first proposed by Birch in 2013[1].

Hospital activity within HES is recorded in three ways (Figure 1):

1. Finished consultant episodes (FCEs)
2. Spells (sequential hospital encounters with different consultants)
3. Continuous inpatient spells (CIPS: hospital admissions for the same patient receiving care from different consultants and different providers/trust within two days after discharge)

FCE is the standard measurement unit for hospital activity and considered to provide more accurate estimates of consultant workload and hospital resources[2]. FCE was used for the basis of analysis and derivation of the TYA CSS to ensure we used all available data on consultant care at the deepest level of granularity available.

Figure 1: Different classifications of hospital admission for an example patient based on HES



Abbreviation: FCEs -finished consultant episodes, CIPs -continuous inpatient spells, A-admission, D- discharge.
Source: Analysing Patient-Level Data Using Hospital Episode Statistics (HES), University of York.

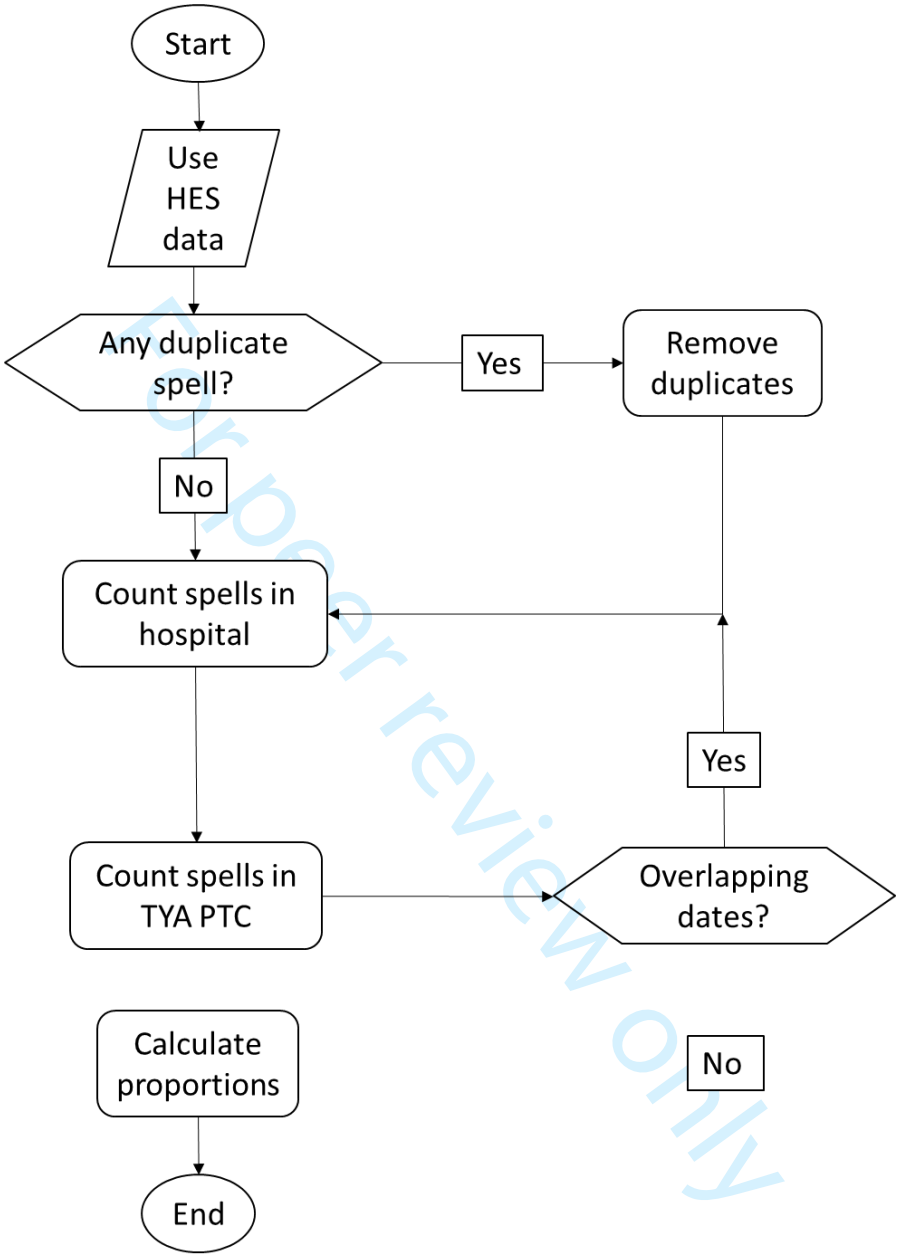
[1] Birch RJ. Teenage and young adult cancer in England – the patient journey and experience. The University of Leeds, PhD Thesis 2013

[2] Hargreaves DS, Viner RM. Adolescent inpatient activity 1999–2010: analysis of English Hospital Episode Statistics data. Archives of disease in childhood 2014; 99: 830-833

BRIGHTLIGHT Cohort profile – supplemental file 2

The development of the TYA CSS is summarised in Figure 2.

Figure 2: Summary of the process for calculating the TYA CSS



Data cleaning

HES data were cleaned to remove duplicates and to clarify some of the diagnostic coding. Reference was made to the HES admitted patient care data dictionary[3] to guide the data cleaning process in order to ensure accuracy and consistency in the recording and analysis of the HES records.

Duplicates were removed to ensure there were not several copies of the same admission being recorded for the same patient. These were identified by ascertaining whether more

[3] HSCIC. HES data dictionary. HEALTH AND SOCIAL CARE INFORMATION CENTRE 2016, 20 January 2016; Available from: http://www.hscic.gov.uk/hesdatadictionary

than one admission began on the same date for a single patient and then cross checking this against admission reasons, procedure codes and treating physician code. Examples of fields which would be indicative of duplicate admission records include multiple HES_IDs, episode start date, episode end date, admission date and discharge date.

Location of specialist care centres

The aim of the study is to evaluate the value of specialist cancer services. 'Specialist' was originally defined in the *Improving Outcomes Guidance (IOG)*[4] as 13 principal treatment centres (PTCs) across England. To account for the age range of the BRIGHTLIGHT cohort starting at 13 years, PTCs also included children's PTCs where the age of admission for the TYA PTC did not include younger adolescents (Table 1). The hospital codes for the look up tables were taken from NHS Digital[5].

Calculation of the scale

The level of specialist care received was calculated from the time of diagnosis (taken from the date recorded in the National Cancer Registration and Analysis Service dataset)

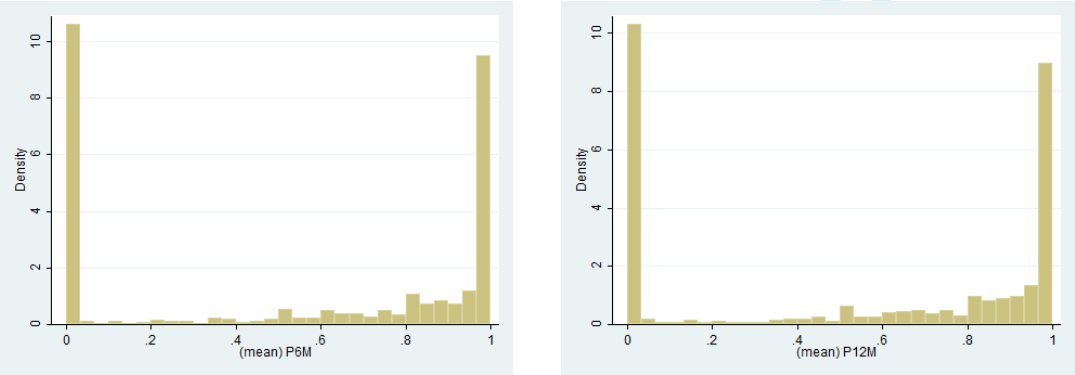
1. Six months after diagnosis: Spells in TYA PTC from diagnosis at 6 months/Total spells from diagnosis at 6 months
2. 12 months after diagnosis: Spells in TYA PTC from diagnosis at 12 months/Total spells from diagnosis at 12 months

For every individual, HES data were used to calculate the number of inpatient and day case bed days spent in a specialist centre (A), as well as the number of total bed days across all secondary care services (B) within the first 6 and 12 months after diagnosis. The proportion of time spent in a specialist centre was then derived as (A)/(B).

Defining the levels of care

Inpatient HES data were successfully linked to 1,074 out of 1,114 young people recruited to BRIGHTLIGHT. The distribution of the proportion of care by 6 months and 12 months after diagnosis suggested there were three natural groups occurring within the data (Figure 3).

Figure 3: Distribution of the proportion of care receive in a TYA PTC



[4] National Institute for Health and Care Excellence. Guidance on cancer services: improving outcomes in children and young people with cancer. NICE, London 2005https://www.nice.org.uk/guidance/csg7/resources/improving-outcomes-in-children-and-young-people-with-cancer-update-773378893 [Accessed 30/08/18]

[5] https://digital.nhs.uk/services/organisation-data-service

BRIGHTLIGHT Cohort profile – supplemental file 2

Table 1: List of principal treatment centres in England (2012-2014) for young people aged 13-24 years

Principal Treatment Centre	**Hospital**
Cambridge University Hospitals NHS Foundation Trust	Addenbrookes Hospital (aged 14-24)
The Christie NHS Trust	Christie Hospital (aged 16-24)
Manchester University Hospitals NHS Foundation Trust	Royal Manchester Children's Hospital (aged 13-15)
Clatterbridge Centre for Oncology NHS Foundation Trust	Clatterbridge Centre (aged 16-24)
Alder Hey Children's NHS Foundation Trust	Alder Hey Children's Hospital (aged 13-19)
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Royal Liverpool Hospital
Royal Liverpool and Broadgreen University Hospital NHS Foundation Trust	Broadgreen Hospital
Leeds Teaching Hospitals NHS Trust	Leeds General Infirmary (aged 13-16)
Leeds Teaching Hospitals NHS Trust	St James's University Hospital (aged 17-24)
Nottingham University Hospitals NHS Trust	City Campus (aged 18-24)
Nottingham University Hospitals NHS Trust	Queens Medical centre (aged 13-18)
Sheffield Teaching Hospitals NHS Foundation Trust	Weston Park Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Royal Hallamshire Hospital (aged 16-24)
Sheffield Teaching Hospitals NHS Foundation Trust	Sheffield Children's Hospital (aged 13-16)
Southampton University Hospitals NHS Trust	Southampton General Hospital (aged 16-24)
Southampton University Hospitals NHS Trust	Southampton Children's Hospital (aged 13-15)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Northern Centre for Cancer Care (aged 19-24)
The Newcastle-upon-Tyne Hospitals NHS Foundation Trust	Royal Victoria Infirmary (aged 13-18)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Sutton (aged 13-24)
The Royal Marsden NHS Foundation Trust	The Royal Marsden Fulham (aged 17-24)
University College London Hospitals NHS Foundation Trust	University College Hospital (aged 13-24)
University College London Hospitals NHS Foundation Trust	Cancer Centre (aged 13-24)
University Hospital Birmingham NHS Foundation Trust	Queen Elizabeth Hospital (aged 16-24)
Birmingham Children's Hospital NHS Trust	Birmingham Children's Hospital (aged 13-18)
University Hospital Bristol NHS Foundation Trust	Bristol Haematology & Oncology Centre (aged 17-24)
University Hospital Bristol NHS Foundation Trust	Royal Hospital for Children (aged 11-16)
University Hospital Bristol NHS Foundation Trust	Bristol Royal Infirmary
University Hospital Bristol NHS Foundation Trust	St Michael's Hospital
University Hospitals of Leicester NHS Trust	Leicester Royal Infirmary (aged 13-24)
Oxford University Hospital NHS Trust	Churchill Hospital (aged 18-24)
Oxford University Hospital NHS Trust	John Radcliffe Children's Hospital (aged 13-18)

BRIGHTLIGHT Cohort profile – supplemental file 2

Supplementary File 2: Development of the BRIGHTLIGHT Severity of Illness Index (BRIGHTLIGHT SIX)

Rationale for developing a bespoke severity index

Within the BRIGHTLIGHT cohort, place of care was not randomly assigned but instead determined by local pathways of care, key influences including the type of cancer, age, proximity to principal treatment centres. As a consequence, differences exist between those who have all/some of their treatment in the teenage and young adult (TYA) Principal Treatment Centre (PTC) and those who have had no care in a TYA PTC. This fundamental difference between the populations of patients who receive no, some or all TYA PTC care was thought likely to be a major confounder in the interpretation of any observed differences in patient experience and outcome between these groups. The differences may not be reflected accurately if cases were grouped solely by, say, tumour type or disease stage due to the considerable variation between tumour types and between similar tumours of different stages in the intensity of treatment received and the likelihood of survival. To interpret the significance of any observed differences in our primary or secondary outcome measures across the populations with no, some or all TYA PTC care, we needed a measure that would allow comparison across patients with different tumours, but capable of discriminating between patient populations. Our primary outcome was quality of life (QOL) and a powerful determinant of QOL is 'the burden of cancer' patients had at diagnosis[1]. We wished to consistently and systematically describe the burden of cancer to assist analysis. The severity of illness index therefore needed to reflect prognosis, disease morbidity (symptoms, physical impact) and treatment morbidity (determined by treatment duration, intensity and anticipated late morbidity burden).

The BRIGHTLIGHT Severity of illness index (SIX)

Constructing the index

All cancer types were compared by symptom burden, treatment burden and prognosis using germ cell tumours as a reference: Stage 1 – very likely to survive, treatment either surgery alone or surgery plus a limited burden of chemotherapy, few if any anticipated late effects of treatment; Stage 2-3 – ~90% survival, many have intensive or multimodality treatment or larger operations, some late toxicity burden; Stage 4 – 50% survival and intensive treatment. Stage 4 we classed as 'most severe' and used this as a reference point to compare odds of survival and treatment burden for other cancers.

Germ cell tumours were chosen as a reference because they are relatively common in the TYA age group, have a range of prognoses from excellent to poor, and treatments have a range of morbidity from surgery alone through to very intensive chemotherapy with both acute and long-term sequelae.

[1] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

BRIGHTLIGHT Cohort profile – supplemental file 2

Three clinicians and two BRIGHTLIGHT researchers reviewed all cancer types to consider allocation to one of three severity levels. Survival estimates were based on examination of current or recently completed trial protocols where available and using a recently published comprehensive TYA-specific reference textbook[2]. We evaluated treatment burden using duration and expected toxicity from multiple sources, including clinical experience, trial protocols, a current TYA oncology text book and international guidelines (such as the National Comprehensive Cancer Network). In addition, other potentially comparable clinical severity scales were sought from the literature to determine comparability or utility in this context.

Content validity of the index

Once a preliminary scale had been constructed, its content was tested by expert review. At least two additional clinicians with specialist clinical expertise were approached to review each tumour type. The reviewers were sent a short document outlining the purpose of the scale and its development to that point as well as the scale itself. They were interviewed either face-to-face or by telephone by a senior clinician and BRIGHTLIGHT researcher (JSW) and asked to respond to two questions:

1. *Within the row(s) of the cancer types in which you have particular expertise (e.g. central nervous system tumours), do you agree with the allocation of grades of severity?*
2. *Looking at other tumour types, by comparison with other rows, do you agree with the allocation of grades of severity?*

Interviews were recorded and field notes taken. The scale was adjusted in response to expert comments to produce a final version (main paper, Table 2).

Applying the BRIGHTLIGHT SIX

BRIGHTLIGHT researchers (RMT, LAF, DS) independently allocated a severity level to each patient, conducting these assessments blind to responses to the survey, including QOL results. Comparisons between the three scores were made and, where there were differences, adjudication through a fourth researcher (JW) determined whether this was an error or due to ambiguity in the Index.

Other measures of severity

We found only one other example in which investigators had categorised TYA by cancer severity. Husson et al[1] used expected 5-year survival to divide patients into three groups, those with expected survival of greater than 80%, 50-80% and less than 50%.[3] Using the same source data[4], we also allocated each patient from the BRIGHTLIGHT cohort a second severity level based on 5-year survival.

We compared this method (Five year survival index, FYX) with BRIGHTLIGHT SIX. As anticipated, those judged to have the most severe cancer by BRIGHTLIGHT SIX are

[2] Bleyer, Barr, Ries, Whelan, Ferrari eds. Cancer in Adolescents and Young Adults. Springer International Publishing, Switzerland 2017

[3] Husson O, Zebrack BJ, Block R, Embry L, Aguilar C, Hayes-Lattin B, Cole S. Health-Related Quality of Life in Adolescent and Young Adult Patients With Cancer: A Longitudinal Study. J Clin Oncol 2017;35:652-659

[4] Bleyer, A. (2011). "Latest Estimates of Survival Rates of the 24 Most Common Cancers in Adolescent and Young Adult Americans." J Adolesc Young Adult Oncol 1(1): 37-42.

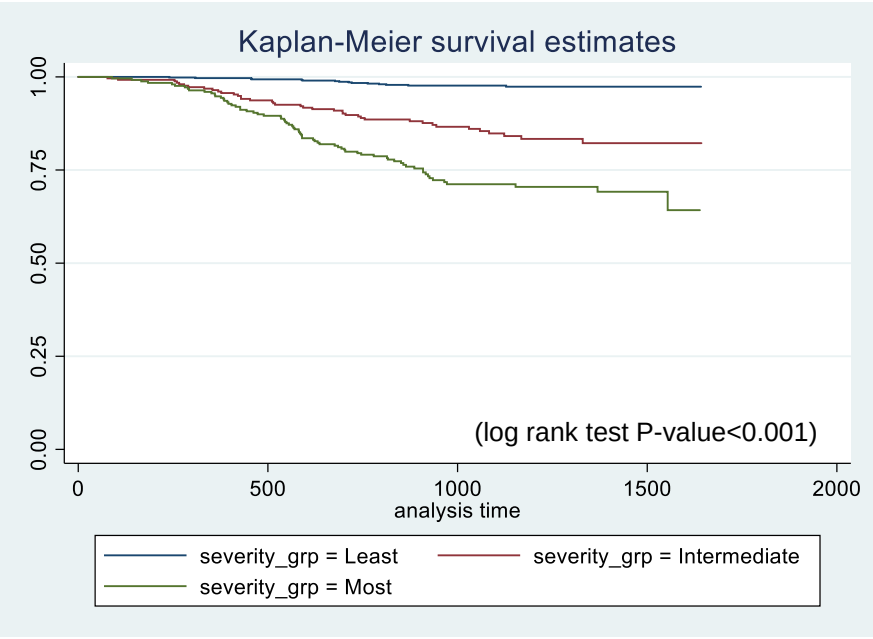
distributed across the three survival categories though weighted towards the two lower survival groups. Similarly, most but not all of those with the least severe cancer by BRIGHTLIGHT SIX had the best expected survival. Those with intermediate severity cancer are spread across the three FYX groups (Table 1).

Table 1: Comparison between the Five year survival Index (FYX) and BRIGHTLIGHT Severity of Illness Index (SIX)

	SIX level		
FYX	Least	Intermediate	Most
<50%	1	100	71
50-80%	56	98	171
>80%	546	56	7

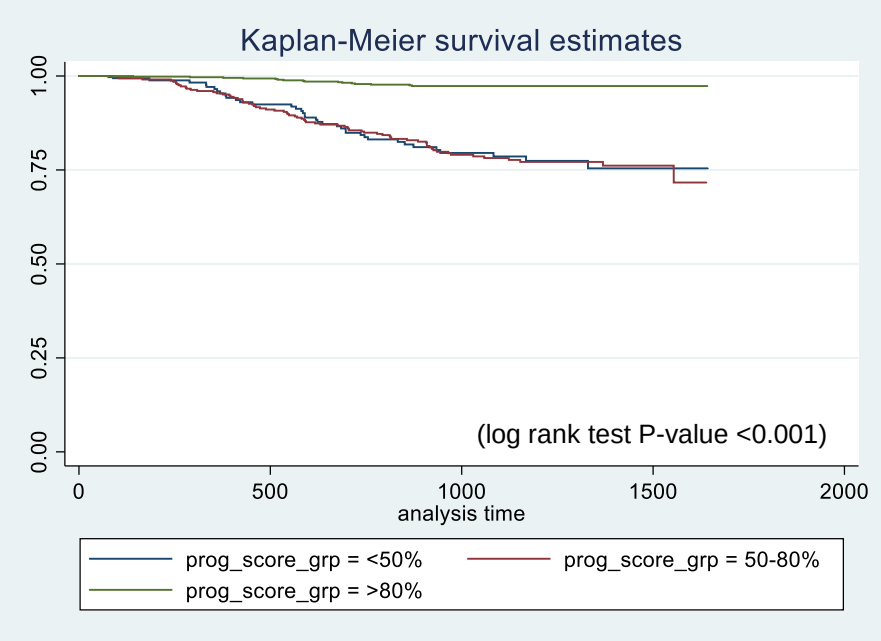
We then analysed survival of the BRIGHTLIGHT cohort using the two indices. Figure 1 demonstrated a clear discrimination in survival by BRIGHTLIGHT SIX, consistent with anticipated survival being an important but not sole component of the index. The survival of the BRIGHTLIGHT cohort was then examined by allocated FYX category (Figure 2). FYX failed to distinguish three groups with distinct survival as that of those allocated to the two lower categories was superimposed.

Figure 1: Survival by BRIGHTLIGHT Severity of Illness Index



BRIGHTLIGHT Cohort profile – supplemental file 2

Figure 2: Survival of BRIGHTLIGHT cohort against allocated FYX group



STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any pre-specified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-9*
Bias	9	Describe any efforts to address potential sources of bias	7
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	Not applicable
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	Not applicable – only reporting baseline

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	characteristics
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 2
		(b) Give reasons for non-participation at each stage	Figure 2
		(c) Consider use of a flow diagram	Figure 2
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	Tables 3-5
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable, presenting wave 1 data only
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable – wave 1 descriptive data only
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	Not applicable
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Descriptive data only presented
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable
Discussion			
Key results	18	Summarise key results with reference to study objectives	18
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19
Generalisability	21	Discuss the generalisability (external validity) of the study results	18-19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	25

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.