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Longitudinal cohort study of the impact of specialist cancer services for teenagers and young adults on quality of life: outcomes from the BRIGHTLIGHT study

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ABSTRACT

Objectives: In England, healthcare policy supports specialised age-appropriate services for teenagers and young adults (TYA), broadly those aged 13-24 years at diagnosis. Specialist Principal Treatment Centres (PTC) provide enhanced age-specific care for TYA, although many still receive their care in adult or children's cancer services. We present the first prospective structured analysis of quality of life (QOL) associated with the amount of care received in a TYA-PTC

Design: Longitudinal cohort study

Setting: Hospitals delivering in-patient cancer care in England

Participants: 1,114 young people aged 13-24 years newly diagnosed with cancer

Intervention: Exposure to the TYA-PTC defined as patients receiving NO-TYA-PTC care with those receiving ALL-TYA-PTC and SOME-TYA-PTC care.

Primary outcome: quality of life measured at five time points: 6,12,18, 24 and 36-months after diagnosis

Results: Group mean total QOL improved over time for all patients, but for those receiving NO-TYA-PTC was an average of 5.6 points higher (95% CI 2.8-8.5) than in young people receiving SOME-TYA-PTC care, and 4.2 points higher (95% CI 1.1-7.3) compared to ALL-TYA-PTC care. Differences were greatest 6 months after diagnosis, reduced over time, and did not meet the 8-point level that is proposed to be clinically significant. Young people receiving NO-TYA-PTC care were more likely to have been offered a choice of place of care, be older, from more deprived areas, in work, and have less severe disease. However, analyses adjusting for confounding factors did not explain the differences between TYA groups.

Conclusions: Receipt of some or all care in a TYA-PTC was associated with poorer QOL soon after cancer diagnosis, but a more rapid improvement in QOL 3-years after diagnosis. However, these changes were small and may not be clinically significant. Receipt of some care in a TYA-PTC requires further study.

Strengths & limitations of this study

- We present the first national evaluation of a model of care which aims to improve outcomes for teenagers and young adults with cancer.
- We were able to quantify where young people received care through nationally collated hospital activity data so we could objectively assign young people to a group representing the model of care received.
- Analysis of longitudinal data for three years after diagnosis was adjusted for multiple confounding variables, identified from a conceptual model of patient experience, which underpinned data collection in the study.
- The measure quantifying where care was received assumed that all teenage and young adult Principal Treatment Centres provided equivalent facilities and care.
- The cohort comprises 20% of the total young people diagnosed with cancer in England during the time period, which could impact on the generalisability of the results.

INTRODUCTION

Cancer in teenagers and young adults (TYA) is rare, though accounts for an estimated 350,000 new diagnoses globally in young people aged 15-29 and a reported rising incidence rate[1]. Lower survival rates compared to younger children have fuelled many international initiatives aimed to improve outcomes and wellbeing. In particular, the need for specialist age-appropriate care and environments are hailed as a critical component of good cancer care for TYA. However, the effect on clinical outcomes that care in such environments may result in are yet to be described.

Distinct cancer service provision for TYA began in the United Kingdom (UK) in the 1990s [2]. This was initiated by clinician and patient advocacy, promoting principles which responded to young people's reports of care that frequently lacked support for their priorities of progress towards normal life goals and care alongside others of a similar age delivered by professionals who understood young people [3]. Specialised UK National Health Services (NHS) for young people with cancer have been mandated in England since 2005 by National Institute for Health and Clinical Excellence (NICE) guidance [4]. The guidance identified that young people's needs may be poorly met in children's and older adult services working in isolation from each other [5], and that TYA-specific places of treatment and care may be key to achieving better outcomes for young people with cancer [6] due in part to the distinct impact of cancer on young people's wellbeing, such as in the physical, psychosocial and developmental domains [7].

The model of specialised TYA cancer care implemented from 2005 focused on 13 TYA Principal Treatment Centres (TYA-PTC) in England, which had funding to develop specialist

care, including age-appropriate environments and multi-disciplinary teams working with TYA. The guidance directed that those under 19 years were treated in a TYA-PTC. The model for young adults aged 19-24 years was to offer choice to receive care in a TYA-PTC or a local cancer unit if it were designated as able to provide their cancer treatment and at least some aspects of age-appropriate care. By 2010, about two-thirds of those aged 15-18 years and one-third of 19-24-year olds were believed to have contact with a TYA-PTC [8]. While there is an international mobilisation to implement specialist TYA services [3], including in other European countries, Australasia and North America, the impact of such services on clinical outcomes has not been robustly evaluated.

The BRIGHTLIGHT study is a prospective evaluation of the benefits of specialist TYA services in the English NHS. In order to capture the complexity of the delivery of TYA cancer care, it comprised an evaluation from the perspective of the environment of care [9], the workforce delivering care [10] and young people receiving care. BRIGHTLIGHT was developed with extensive input from young people as well as health professionals [6, 11, 12] and based on consultation with young people [13]. This included input into the selection of the primary outcome: quality of life (QOL).

Quality of Life is defined as "…subjective, multidimensional and dynamic. It is unique to each individual and includes aspects of physical, psychological and social function. It is dependent not only upon the stage of development but also the illness trajectory. This involves the achievement of goals and aspirations and the constraints imposed through ill health and treatment" [14]. Measurement of QOL uses the patient's own report to evaluate the spectrum of impact of illness upon them and has become an increasingly valued healthcare outcome. Previous reports of young people's QOL after a cancer diagnosis have shown this to be significantly lower than normative population data [15]. Longitudinal assessment has indicated QOL improved in the first year after diagnosis but there was no significant improvement in the second year [16]. No evaluation beyond the second year has been reported and while studies have investigated predictors of QOL there has been no evaluation of the impact of different models of delivery of care on QOL. We examined QOL at 6, 12, 18, 24 and 36 months after diagnosis in relation to the proportion of care young people received in a TYA-PTC

METHODS

Study design

The BRIGHTLIGHT study is a mixed methods programme of research. Results from an embedded longitudinal cohort study, obtaining data from young people through a bespoke survey [17], are reported here. The survey was administered at five time points during the first three years after diagnosis (6, 12, 18, 24 and 36 months, waves 1-5 respectively). A scale was developed, previously described in detail [18], using Hospital Episode Statistics (HES) in-patient data to measure episodes of care in different NHS Trusts and then used to assign young people to one of three levels of TYA care dependent on how much in-patient HES activity recorded in the first 12 months after diagnosis was delivered in a TYA-PTC: no care in a TYA-PTC (NO-TYA-PTC), some care delivered in a TYA-PTC with additional care in a children's or adult cancer unit (SOME-TYA-PTC) or all care delivered in a TYA-PTC (ALL-TYA-PTC).

Participants and setting

BRIGHTLIGHT was open to recruitment between October 2012 and April 2015 in 109 English NHS hospitals of which 97 recruited at least one young person. Eligibility was defined as aged 13-24 years at the time of diagnosis, newly diagnosed with cancer (ICD-10 codes C00-C97) and recruited within four months of diagnosis. There was no eligibility exclusion for a language or sensory impairment affecting communication. The following groups were excluded: those serving a custodial sentence; not anticipated to be alive at the first point of data collection (6-months after diagnosis); or incapable of completing a survey. Details of the recruitment process are reported elsewhere [18, 19]. Young people gave written consent and parental consent was also obtained for those less than 16 years. Checks were made through the Demographic Batch Service at NHS digital before each wave of data collection to ensure young people were alive and to obtain their most recent address. The study was approved by London-Bloomsbury NHS Research Ethics Committee and the Confidentiality Advisory Group of the Health Research Authority.

The sample size calculation was based on a comparison between the three levels of TYA care [18] for the primary outcome of PedsQL total score [20], measured at five time points over the three-year follow-up. Previously reported PedsQL data for childhood cancer patients suggested a standard deviation for this score of 16 [21]. To detect a difference in scores of 8 units with 80% power [22] required a sample of 200 young people. This calculation assumed a significance level of 0.01 (2 sided) to allow for multiple comparisons between three levels of TYA care and assumed an average of three repeated measurements per patient (intra cluster correlation 0.3 as suggested as a maximum for similar patient outcomes [23]). The calculation allowed for adjustment for confounding factors using a variance inflation factor with a correlation of 0.5 [24]. To ensure adequate power to examine the effect of TYA care on QOL within subgroups of age at diagnosis (13-18 and 19-24 years) and type of tumour (haematological, solid tumour groups), the minimum required sample size was raised to 800 (80% power).

Data collection

Data were collected from three sources: young people's self-report, patient clinical records, and NHS and Public Health England (PHE) databases. Details of these data sources are reported elsewhere [18]. Data presented here are responses to the BRIGHTLIGHT Survey, a bespoke survey containing five validated questionnaires and 169 descriptive questions related to post diagnosis experience. The survey was administered through face-to-face interviews in young people's homes by an independent research company at the first time point and either online or telephone interview at subsequent waves of data collection [17].

This paper reports data for the primary outcome, QOL, which was measured using the Pediatric Quality of Life Questionnaire (PedsQL) [20]. At the time of study development this was the only measure of QOL validated for teenagers and young adults [25]. It contains 23 items rated using a five-point Likert Scale (Never, Almost never, Sometimes, Often, Almost always). Responses are presented as four domain scores (physical, emotional, social, and work/studies functioning), two summary scores (physical and psychosocial function) and a total score. Domain, summary and total scores range from 0-100, with 100 representing the best possible QOL.

Analysis

Analysis was carried out following a predefined statistical analysis plan using STATA version 15. A mixed effects model was used to investigate the relationship between the levels of TYA care and the PedsQL total score, allowing for repeated measurements taken over the 3 years since diagnosis. The model was adjusted for confounding factors identified based on the conceptual model underpinning the BRIGHTLIGHT Survey [11, 17] and using a causal diagram in the form of a Directed Acyclic Graph (DAG) (DAGitty software www.dagitty.net; Supplemental File, Figure A1). Factors adjusted for were age at diagnosis, type of cancer (leukaemia, lymphoma, brain and central nervous system, bone tumours, sarcoma, germ cell, melanoma, carcinomas, other), socioeconomic status (Index of Multiple Deprivation (IMD) [26] quintile), severity of cancer (least, intermediate, most [18]), ethnicity (white, other), choice offered about where to receive treatment (yes/no), presence of any long term condition prior to cancer (yes/no), days from first symptom to diagnosis and number of General Practitioner visits before diagnosis. Geographical location (specified as 12 cities, derived from the TYA-PTC and their network of hospitals) was included in the model as a random effect. Models were extended to include interaction terms to investigate predefined subgroup effects by age at diagnosis (both as a continuous factor and using categories of 13-18 and 19-24 years) and tumour type (haematological and solid tumours). An interaction with time since diagnosis was also examined to investigate whether the relationship between level of TYA care and QOL changed over time. Similar models were fitted for the PedsQL domain scores for physical, social, emotional and work/school/college functioning, and the psychosocial summary score.

The extent and patterns of missing QOL data over time was examined using summary statistics and profile plots. As there is no provision in the scoring of PedsQL to directly account for death, our main analysis did not distinguish between data 'missing' following death and that missing for other reasons. With the possibility of informative missing data due to deaths, a sensitivity analysis was carried where joint mixed-effect models for the longitudinal QOL scores and time until death were fitted to account for the correlation between the QOL and survival outcomes [27]. The QOL estimates for the effect of level of TYA care were then compared with those obtained from previously fitted mixed models.

RESULTS

A total of 1,126 young people were recruited. BRIGHTLIGHT survey data at wave 1 were available for 830 (75%) participants and details of numbers at each wave are summarised in Figure 1. Characteristics of those who did and did not complete wave 1 were similar, except for a higher proportion of non-white participants not completing wave 1 (12% vs. 19%, p=.004) [18]. Forty-eight participants could not be assigned a level of TYA-PTC care as there were no linked HES in-patient records available. Data from 782 young people were therefore included. There were fewer young people receiving ALL-TYA-PTC care (n=193; 25%) in comparison to SOME-TYA-PTC (n=312; 40%) and NO-TYA-PTC (n=277; 35%). Demographic characteristics and summary of variables adjusted for in the analysis are shown in Table 1. Young people who received NO-TYA-PTC care were slightly older, more likely to be working full/part time, had less severe disease, had a better prognosis and were more likely to have been given a choice in their place of care. Young people who had ALL-TYA-PTC care were more likely to come from less deprived areas.

Table 1: Participant characteristics according to level of care at wave 1

Characteristic		Level of TYA care at 12 months from diagnosis		
		NO-TYA-PTC N=277	**SOME-TYA-PTC N=312**	**ALL-TYA-PTC N=193**
Age at diagnosis (years)	Mean (SD)	21.04 (3.01)	19.40 (3.41)	19.97 (3.15)
Gender	Male	148 (53%)	165 (53%)	112 (58%)
	Female	129 (47%)	147 (47%)	81 (42%)
Ethnicity*				
	White	252 (91%)	273 (88%)	163 (84%)
	Mixed	4 (1%)	5 (2%)	4 (2%)
	Asian	15 (5%)	24 (8%)	20 (10%)
	Black	4 (1%)	7 (2%)	2 (1%)
	Other	2 (1%)	3 (1%)	4 (2%)
Socioeconomic status (IMD quintile)				
	1 – most deprived	66 (24%)	73 (24%)	34 (18%)
	2	47 (17%)	52 (17%)	32 (17%)
	3	51 (19%)	60 (20%)	37 (20%)
	4	65 (24%)	61 (20%)	40 (21%)
	5 – least deprived	46 (17%)	59 (19%)	46 (24%)
Marital Status				
	Married/civil partnership	9 (4%)	8 (3%)	6 (3%)
	Cohabiting	43 (17%)	27 (10%)	18 (10%)
	Single/divorced	198 (79%)	227 (87%)	148 (86%)
Current status				
	Working full/part time	126 (45%)	72 (23%)	43 (22%)
	In education	61 (22%)	112 (36%)	81 (42%)
	Other work (apprentice/intern/voluntary)	6 (2%)	5 (2%)	6 (3%)
	Unemployed	10 (4%)	11 (4%)	7 (4%)
	Long term sick	39 (14%)	51 (16%)	31 (16%)
	Not seeking work	35 (13%)	61 (20%)	25 (13%)

Type of cancer (Birch classification)	Leukaemia	19 (7%)	49 (16%)	33 (17%)
	Lymphoma	111 (40%)	75 (24%)	70 (36%)
	CNS	9 (3%)	9 (3%)	12 (6%)
	Bone	7 (3%)	59 (19%)	3 (2%)
	Sarcomas	8 (3%)	31 (10%)	15 (8%)
	Germ cell	64 (19%)	55 (18%)	31 (16%)
	Skin	22 (8%)	1 (<1%)	4 (2%)
	Carcinomas (not skin)	41 (15%)	31 (10%)	23 (12%)
	Miscellaneous specified**	5 (2%)	2 (<1%)	1 (<1%)
	Unspecified Malignant	1 (<1%)	0	1 (<1%)
Severity at diagnosis (row %, column %)	Least	200 (46%, 72%)	133 (31%, 43%)	95 (22%, 49%)
	Intermediate	49 (26%, 18%)	82 (44%, 26%)	56 (30%, 29%)
	Most	28 (17%, 10%)	97 (58%, 31%)	42 (25%, 22%)
Prognostic score	<50%	21 (8%)	60 (19%)	41 (21%)
	50-80%	54 (20%)	125 (40%)	44 (23%)
	>80%	200 (73%)	126 (41%)	108 (56%)
Location* **	Birmingham	41 (15%)	59 (19%)	12 (6%)
	Bristol	51 (18%)	32 (10%)	4 (2%)
	Cambridge	12 (4%)	8 (3%)	1 (1%)
	Manchester	22 (8%)	35 (11%)	11 (6%)
	Merseyside	13 (5%)	11 (4%)	6 (3%)
	East Midlands	15 (5%)	24 (8%)	60 (31%)
	Leeds	20 (7%)	25 (8%)	25 (13%)
	Newcastle	13 (5%)	6 (2%)	24 (12%)
	Oxford	5 (2%)	4 (1%)	7 (4%)
	London	60 (22%)	83 (27%)	10 (5%)
	Sheffield	7 (3%)	9 (3%)	9 (5%)
	Southampton	18 (7%)	16 (5%)	24 (12%)

Given a choice about where to receive treatment[$]	Yes No (or < 19 years)	N=272 121 (45%) 151 (56%)	N=311 86 (28%) 225 (72%)	N=192 48 (25%) 144 (75%)
Long term condition prior to cancer	Yes No	N=277 20 (7%) 257 (93%)	N=311 34 (11%) 277 (89%)	N=193 18 (9%) 175 (91%)
Time to diagnosis: days from 1st symptom	Median (IQR), [min, max]	N=264 62 (29·5 to 168·5) [0, 1340]	N=304 65·5 (29·5 to 152·5) [0, 959]	N=188 63·5 (25·5 to 151·0) [0, 1217]
Time to diagnosis: number of GP visits before diagnosis	Median (IQR), [min, max]	N=274 1 (0 to 3) [0, 20]	N=311 1 (0 to 3) [0, 20]	N=193 2 (1 to 3) [0, 40]

* Wave 1 data was used with missing values completed using available PHE data.

** includes 4 'unclassified' – treated in cancer unit but did not have cancer

***Includes the TYA-PTC and hospitals linked to the multi-disciplinary team at the TYA-PTC; where available based on hospital of diagnosis, for 77 cases based on recruiting hospital

$ Those <19 years at diagnosis were assumed not to have been given a choice

Longitudinal changes in the average QOL total score according to the level of care are shown in Figure 2 (summary by wave is given in Supplemental file, Table A1). Across all time periods this illustrates lower QOL score for those in the SOME and ALL-TYA-PTC groups compared to the NO-TYA-PTC group. Differences between level of care appeared to diminish steadily over time. The negative coefficients for levels of care from the model indicate that across the 3 year period of the study QOL scores were on average higher for those with NO-TYA-PTC care compared with SOME-TYA-PTC and ALL-TYA-PTC with a larger difference compared with the SOME-TYA-PTC category (Table 2). The differences were statistically significant but fell inside the threshold of 8 points proposed to be clinically significant [20]. There was no evidence that the relationship between QOL and level of care was different for the combined group of leukaemia/lymphomas compared with other cancers. Also, there was no evidence of a difference by age at diagnosis (Figure 3). There was evidence that the QOL/Level of care relationship changed over time such that differences between the groups diminished i.e. slopes for SOME-TYA-PTC and ALL-TYA-PTC over time are steeper than for NO-TYA-PTC, therefore rates of improvement of QOL were superior in the ALL-TYA-PTC and SOME-TYA-PTC (Table 3), mirroring what was seen in Figure 2. Analysis of the physical functioning and work/school/college functioning domain scores showed a similar pattern to that seen for the total QOL score. For the emotional functioning domain however, difference between groups were less marked and notably the average difference in scores between the SOME-TYA-PTC and NO-TYA-PTC was reduced. Difference between groups in terms of social functioning and the psychosocial summary scores were small and not statistically significant (Figure 4, Table 4).

Table 2: Mixed model investigating the relationship between levels of TYA care received during the first 12 months from diagnosis and quality of life over 3 years (N=733)

		Difference in means	**95% Confidence Interval**	**P-value****
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-5.63	-8.49 to -2.77	P=0.0005
	ALL-TYA-PTC	-4.17	-7.28 to -1.07	

* results from a three level model for repeated measurements of QOL over time since diagnosis, with a random effect for geography and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis. Missing data for 96 due to missing TYA category and missing data in other covariates

** Likelihood ratio test

Table 3: Investigation of changes in QOL score over time: Results from adjusted* mixed effects models with interaction term (time months x TYA-PTC category). Coefficients for time describe the linear increase in QOL score per month within each TYA care category (N=733)

TYA care category	**Coefficient for time (per month)**	**95% confidence interval**	**P-value from interaction**
NO-TYA-PTC	0.26	0.18 to 0.34	0.004
SOME-TYA-PTC	0.45	0.37 to 0.53	
ALL-TYA-PTC	0.37	0.27 to 0.46	

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Table 4: Results from adjusted mixed effects models investigating the relationship between levels of TYA care received during the first 12 months from diagnosis and the quality of life domain scores

		Difference in means	95% Confidence Interval	P-value
PHYSICAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-8.28	-11.95 to -4.61	P=0.0001
	ALL-TYA-PTC	-4.79	-8.76 to -0.81	
EMOTIONAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-4.29	-7.79 to -0.80	P=0.015
	ALL-TYA-PTC	-5.43	-9.29 to -1.57	
SOCIAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-2.96	-5.77 to -0.16	P=0·099
	ALL-TYA-PTC	-2.49	-5.60 to 0.62	
WORK/SCHOOL/COLLEGE FUNCTIONING (N=595)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-6.87	-10.45 to -3.30	P=0.0007
	ALL-TYA-PTC	-4.67	-8.47 to -0.87	
PSYCHOSOCIAL SUMMARY SCORE (N=600)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-2.51	-5.71 to 0.70	P=0.074
	ALL-TYA-PTC	-3.96	-7.44 to -0.48	

** results from a three level model for repeated measurements of QOL domain score over time since diagnosis, with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Results from post hoc analysis excluding patients with bone tumours were similar to those for all cancers combined (Supplemental file, Table A2). A subgroup investigation of patients with lymphoma, the biggest diagnostic category, showed these were not significantly different from those for the group of other cancer types (Supplemental file, Table A3). Finally, sensitivity analyses using joint modelling for survival alongside longitudinal QOL did not alter the conclusion based on the main results (Supplemental file, Table A4).

DISCUSSION

Our study is the first reported national longitudinal evaluation of specialist cancer services, more specifically TYA-PTCs and their networks of care, as they were originally defined in 2005 [4]. We recorded patient outcomes to determine the influence of place of care, and after consultation with patients and professionals, selected QOL as the primary parameter of interest. Using routinely collected hospital admission data to identify time spent in the TYA-PTC, we categorised patients by the level of their care received in the TYA-PTC (all, none or some). We found that there was a statistically significant difference between these groups with those in the NO-TYA-PTC group having superior QOL compared to those in the ALL-TYA-PTC group, whilst those in the SOME-TYA-PTC group reported lowest QOL. Quality of life improved over time in all three groups, but rates of improvement were significantly better for SOME and ALL-TYA-PTC.

We predicted that sociodemographic or disease factors might explain some of the differences between groups and adjusted the analyses for these confounding variables. Despite extensive analysis we were unable to identify other factors to account for these differences. Like other reports of young people's QOL after a cancer diagnosis [15], we found this to be low, irrespective of where young people were treated. We found that young people who did not access a TYA-PTC had better QOL in comparison to those who had all or some of their care in a TYA-PTC. However, while this was statistically significant, the mean difference between the NO-TYA-PTC and ALL-TYA-PTC groups was not at a level proposed as clinically significant (8-point difference [21]). Nevertheless, it is important to consider reasons for lower QOL when young people experience multiple types of place of care and the determinants of place of care. Based on work in other settings where care is delivered on multiple sites [28] we surmise that this may result from limited coordination of care, perhaps including inadequate communication with and between professionals. Having to repeat conversations and explanations of their cancer diagnosis and treatment details is frequently reported as burdensome to young people [11]. A greater understanding of the determinants of place of care for young people and the factors which influence a sense of care co-ordination deserve further exploration.

It is interesting that young people who had no access to the TYA-PTC rated their QOL the highest. This could reflect young people rating themselves by comparison with the other people they could see being treated for cancer outside of a TYA-PTC, including older adults. It could also be that young people chose to receive care locally rather than travel to the TYA-PTC so they could keep their links to their 'normal' life, which is supported by the domain level analysis where they also rated their work/school/college functioning higher. Future work could focus on the influence of being given a choice in the place where young people receive care, and the factors that young people consider to be important when making this decision.

The longest follow-up for longitudinal assessment of QOL previously reported to two years after diagnosis [16], which showed no improvement after the first year. However, we found that there was a gradual improvement in QOL over 3-years, which was more rapid when young people received all their care in a TYA-PTC. The philosophy of TYA cancer care includes the delivery of care to support young people to achieve their long-term personal outcomes (education, employment and relationships), the benefits of care provided by the TYA-PTC may therefore not be realised in the short-term. It would be beneficial for us to understand whether this improvement continued into long-term survivorship, especially the influence of QOL reaching and sustaining goals such as employment.

There are several limitations to this study including how specialist care was defined and measured. This was based on the location of the 13 NHS Trusts in England commissioned as TYA-PTCs but not the specific hospitals within these Trusts where the specialist TYA services were based. For example, a Trust which included multiple hospitals could only have specialist TYA services in one therefore a young person receiving care in one of the other hospitals was assumed to have had access to specialist TYA services. Furthermore, using the Trust commissioned as a TYA-PTC does not capture the details of the TYA-specific care available or delivered and assumes that this is equal in all. We know there was wide variation in the delivery of care through the duration of the study [29]. However, at the time of study inception HES was the sole data source available that would allow an objective

measurement of place of care. In complementary work, the key elements of specialist age-appropriate care for TYA have been described [9]. This would provide an alternative categorisation against which to measure patient and clinical outcomes.

The cohort represented approximately a fifth of the total cancer population diagnosed between July 2012 and December 2014 as ascertained through the National Cancer Registration and Analysis Service, and there were differences in cancer types between the cohort and those not recruited [18], which could impact on the generalisability of the results. We used a single mode of survey administration at wave 1, and multiple modes at waves 2-5. While this may have introduced a social desirability bias (noted to be more so for telephone interviews than web-based surveys [30]), this was to increase the response rate as work during the feasibility study for BRIGHTLIGHT indicated no one method was acceptable to all young people. Finally, we used a measure of QOL that was validated across the age 13-24 years [25], but this may not reflect the issues that were most relevant to young people with cancer in the UK (having been developed in the US in a non-cancer population). This is supported by comments made in the cognitive interviews undertaken when the survey was being developed; young people did not agree with the wording of the school functioning domain, so this was changed to work/school/college [17]. However, young people who were not in education, employment or training would not be able to answer these questions. Future work is required to develop TYA-specific QOL measures that reflect issues specific to this population.

Despite these limitations this is the first systematic prospective evaluation of specialist services for young people with cancer. We have found that TYA cancer care as commissioned in 2010 resulted in young people's QOL gradually improving 3-years after diagnosis and improving more rapidly from a lower baseline if young people's treatment involved a TYA-PTC. NHS care pathways may result in care in specialist centres for young people with the poorest initial QOL, and local care for those with the least poor initial QOL, risk stratifying the patients appropriately. Young people who receive some care in both a children's or adult cancer unit and at a TYA-PTC also have an improvement in QOL, but the rate of improvement was less and QOL remained lower than for young people treated in a single type of organisation. The factors influencing place of care and the differences in QOL and survival remain unclear. A model of 'joint care', increasing the emphasis and investment in communication between TYA-PTCs and other Trusts designated to deliver elements of TYA cancer care, is currently proposed by the NHS in England. The influence of such changes in care provision should be examined prospectively in future to identify if QOL of young people with cancer is improved wherever care is received.

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Author contributions:
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.

Patient and public involvement:
Young people have been involved in this study from the feasibility stage onward. They were involved in study development, acted as co-researchers and were instrumental in the design and methods of the study. A representative of the Young Advisory Panel (YAP) was a co-applicant on the grant and the YAP have been part of the management of the study since the grant was awarded in 2011. Details of the extent of young people's involvement in BRIGHTLIGHT is provided in reference 13.

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Competing interests:
None declared.

Ethics Approval:
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Data sharing statement:

Further details of the BRIGHTLIGHT programme of work are 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 2020 when the primary analysis is complete. We welcome collaboration, for general data sharing enquiries please contact RMT (rtaylor13@nhs.net).

Final version

Figure legends

Figure 1: Participation at each wave of data collection

*Drop-outs between waves due to death, permanent optout 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 2: Mean PedsQL total score over time since diagnosis (with 95% confidence intervals)

Graph based on data collected in Waves 1 to 5, plotted against median time since diagnosis.

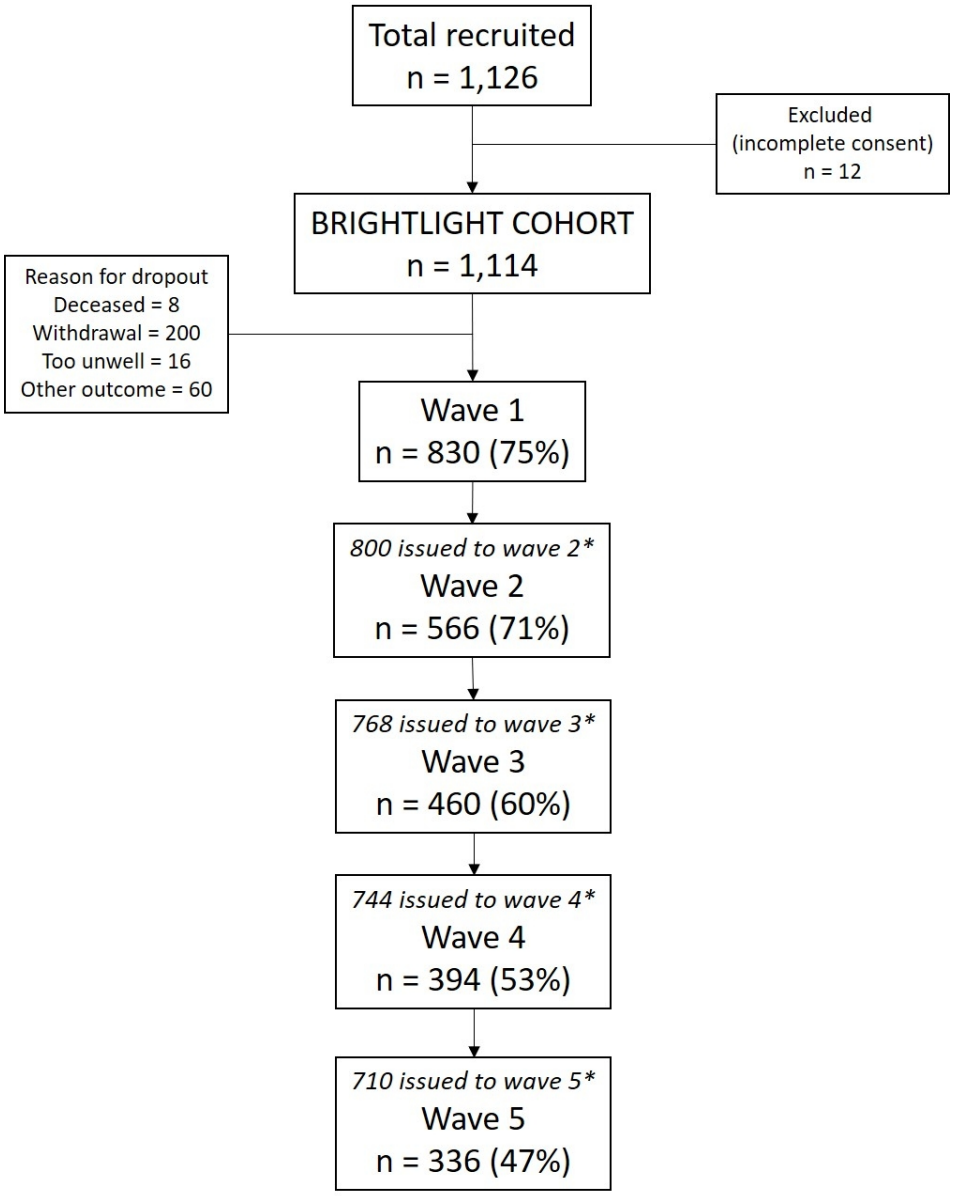
Figure 3: Subgroup investigations for cancer type (leukaemia/lymphoma v other) and age group (<19 v 19+): Results from adjusted* random effects models with interaction terms (N=733)

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, Choice about where to receive treatment, Long term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Figure 4: Mean PedsQL domain scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 4a: Physical functioning
Figure 4b: Emotional functioning
Figure 4c: Social functioning
Figure 4d: Work/school/college functioning
Figure 4e Psychosocial summary score



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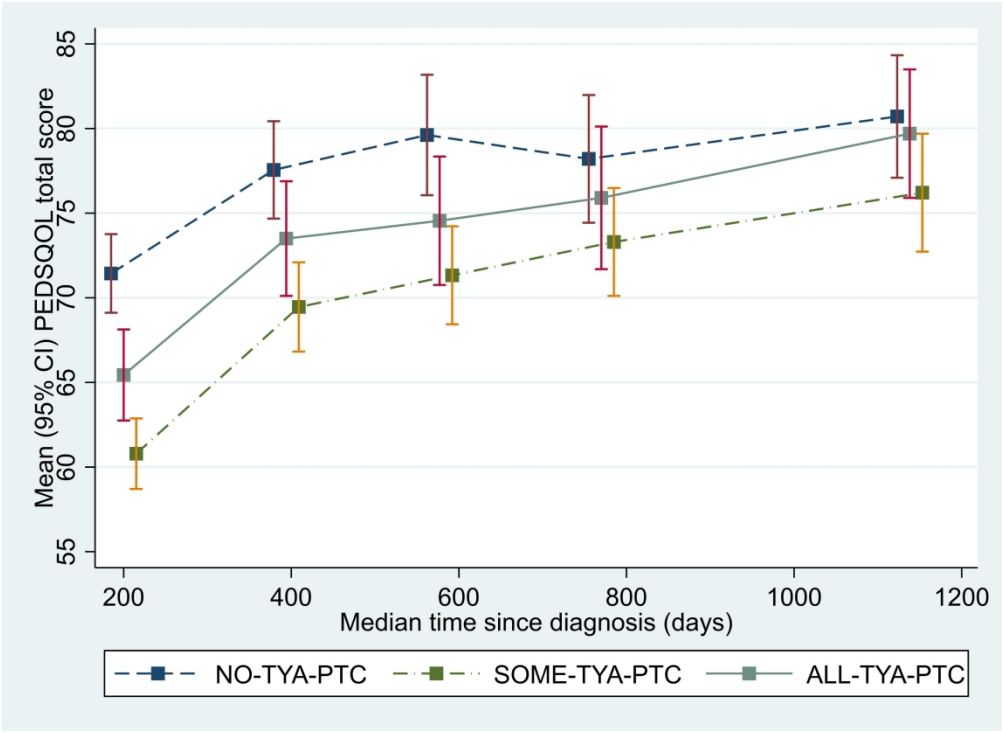

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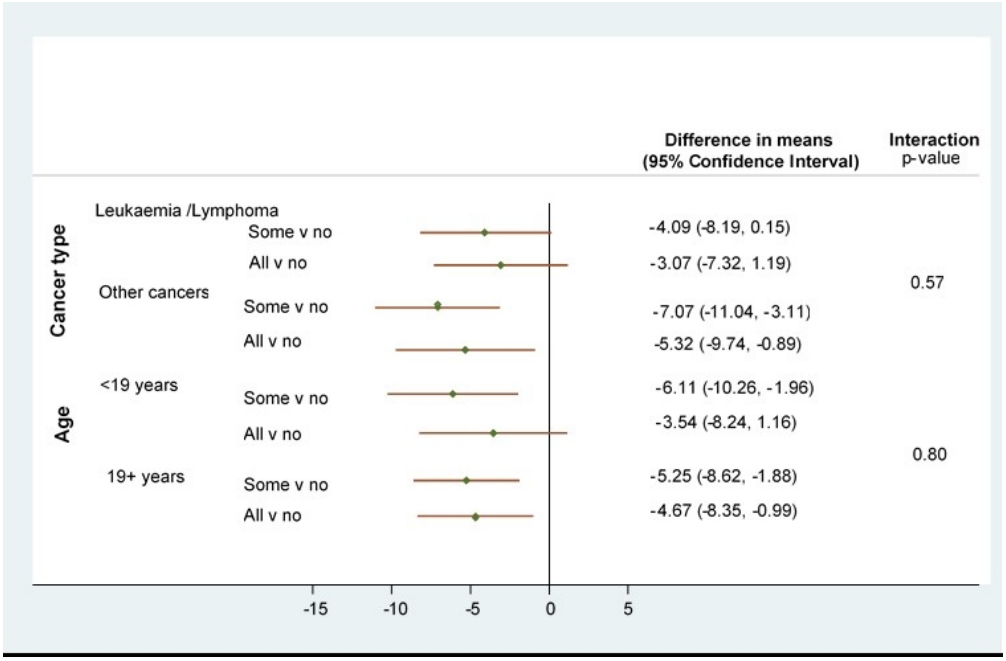

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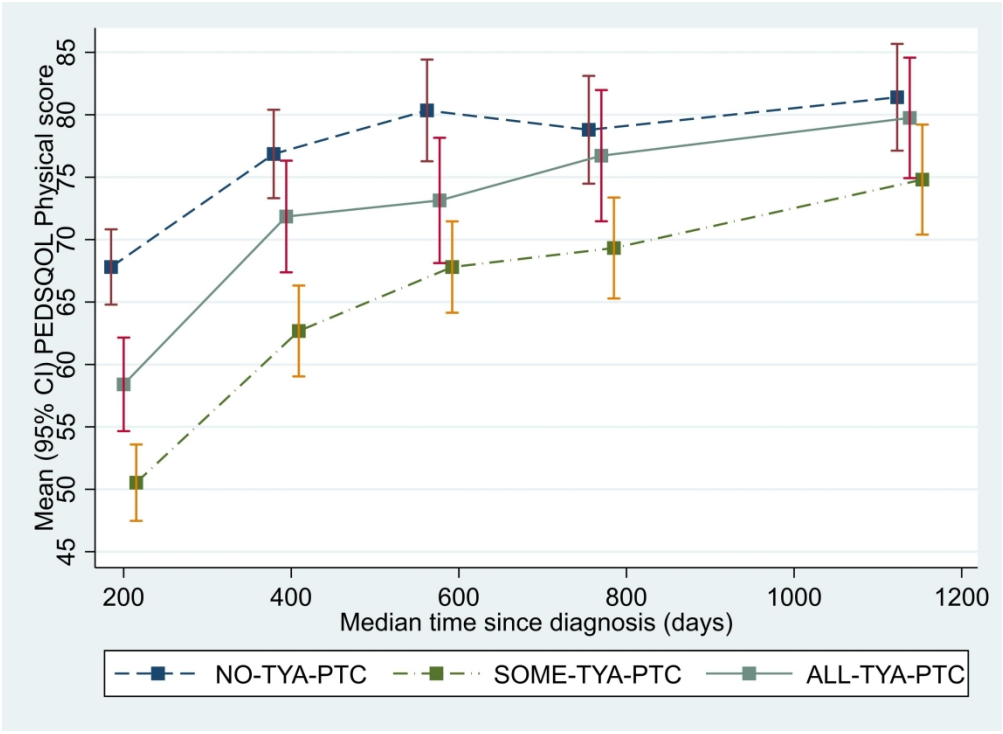

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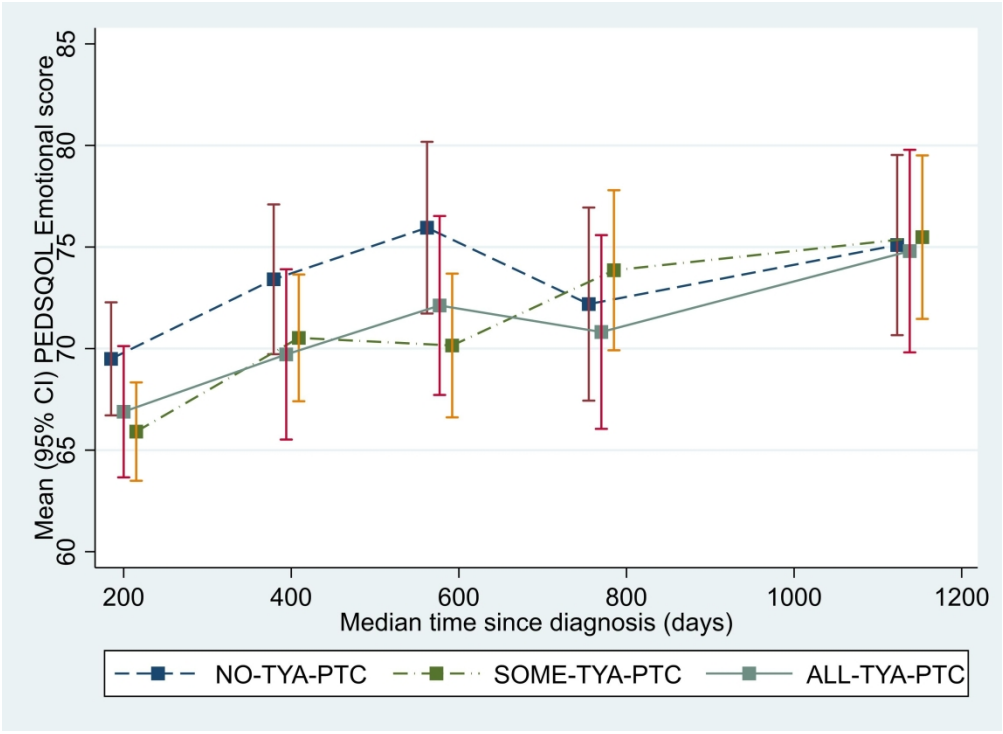

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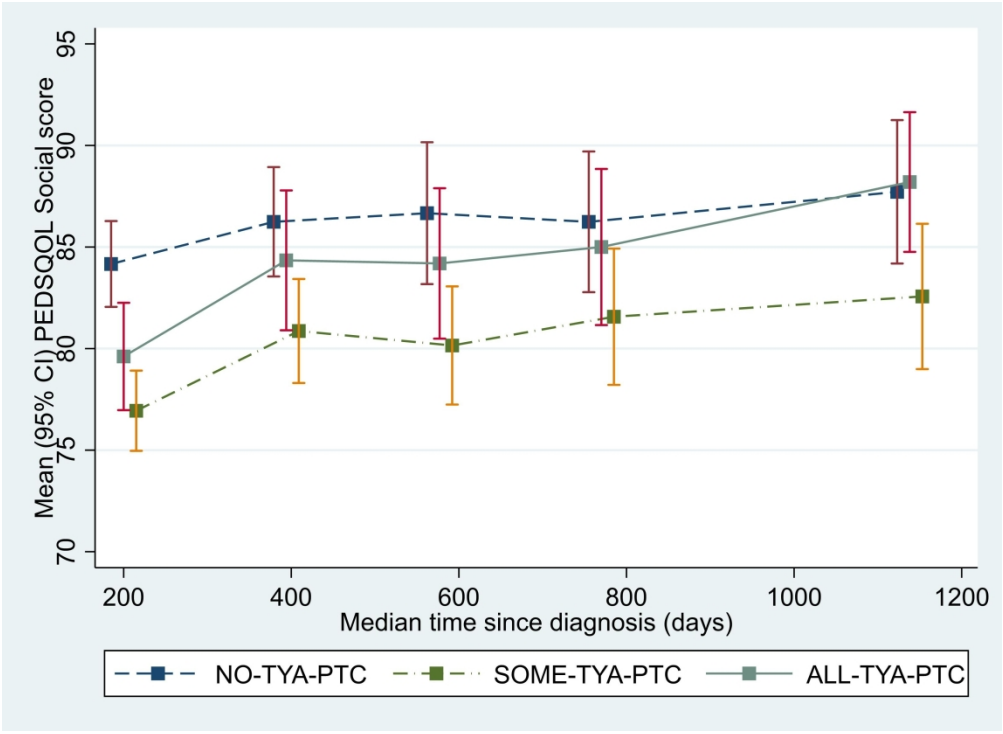

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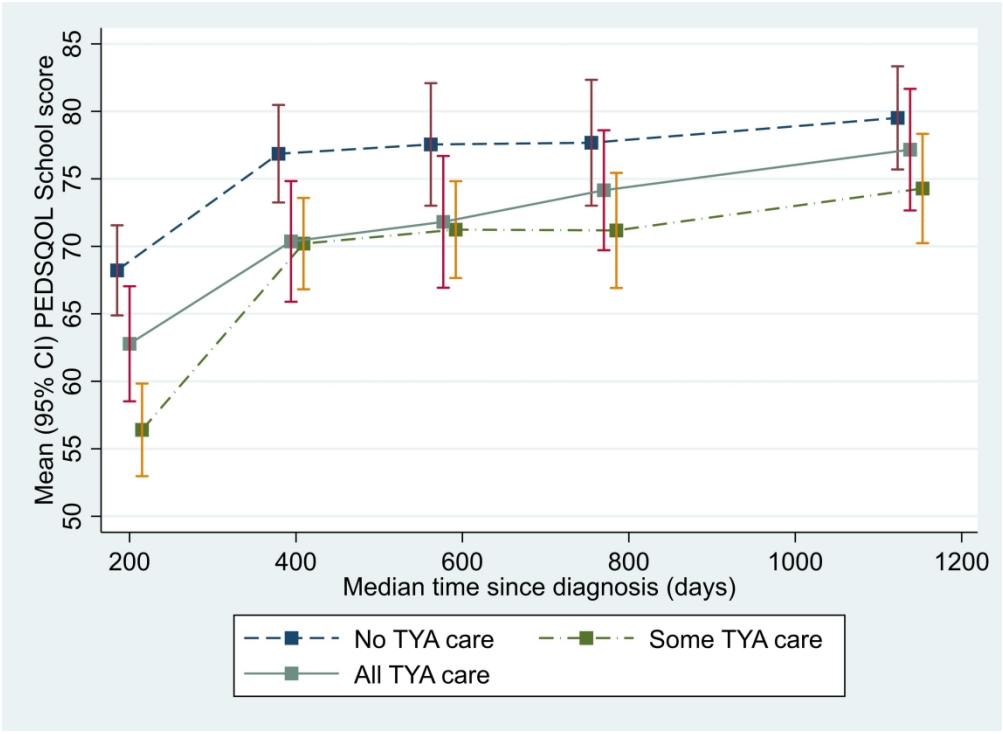

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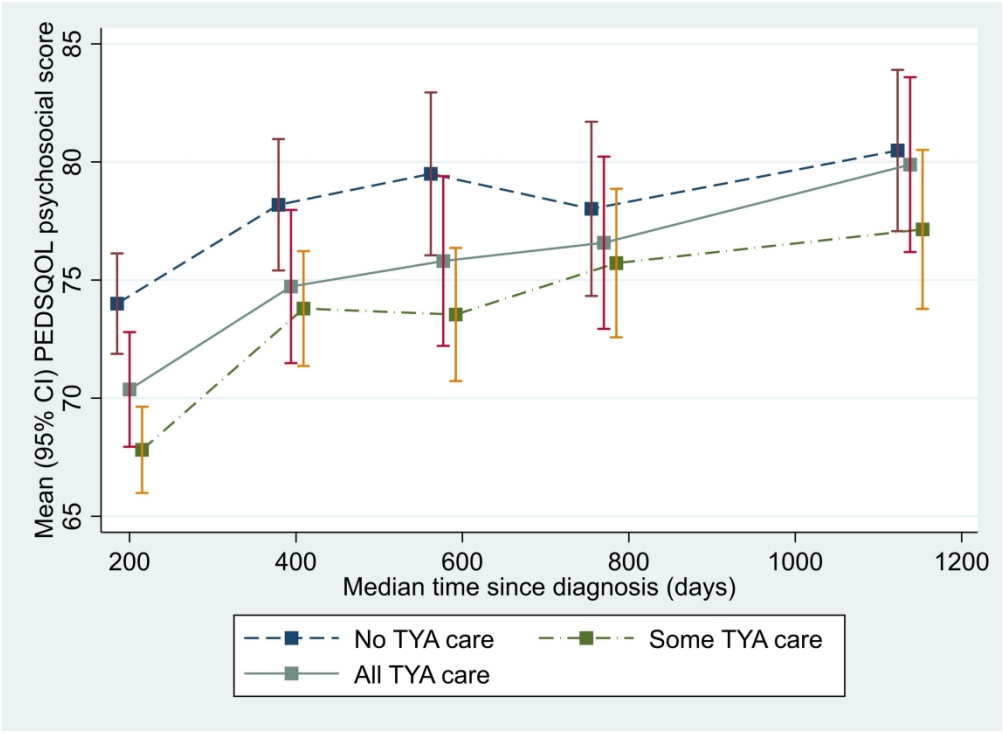

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Supplemental file

Figure A1: Matrix representing the causal diagram explaining confounding variable to enter in the Directed Acyclic Graph (DAG)

	TYA SCL	QOL	Age	Choice	CS	CT	DoH	Ethnicity	Finances	Gender	Geography	I&C	LTC	RtD	SE	SES	SS
TYA SCL		⇗	⇙	⇙	⇙	⇙	⇗	⇙	⇙	O	⇙	⇗	⇙	⇙	⇗	⇙	⇗
QOL			⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙	⇙
Age				⇗	O	⇗	⇗	O	⇗	O	O	⇗	⇗	⇗	⇗	⇗	⇗
Choice					⇙	⇙	O	⇙	⇗	O	⇙	⇗	⇙	⇙	⇗	⇙	⇗
CS						⇙	⇗	⇙	⇗	O	⇙	⇗	⇙	⇙	⇗	⇙	⇗
CT							⇗	⇙	⇗	⇙	⇙	⇗	⇙	⇗	⇗	⇙	⇗
DoH								⇙	⇙	⇙	⇙	⇗	⇙	⇙	⇗	⇙	⇗
Ethnicity									⇗	O	⇙	⇗	⇗	⇗	⇗	⇗	⇗
Finances										O	⇙	⇙	⇙	⇙	O	⇙	⇙
Gender											O	⇗	⇗	⇗	⇗	O	⇗
Geography												⇗	⇗	⇗	⇗	⇗	⇗
I&C													⇙	⇙	⇗	⇙	⇗
LTC														⇗	⇗	⇙	⇗
RtD															⇗	⇙	⇗
SE																⇙	⇗
SES																	⇗
SS																	

CS: cancer severity; CT: cancer type; DoH: duration of hospitalisation; I&C: information & communication; LTC: long-term condition; QOL: quality of life; RtD: route to diagnosis; SE: symptom experience; SES: socioeconomic status; SS: social support

O – indicates a null relationship

Table A1: PedsQL total score by Wave of data collection

	NO-TYA-PTC			SOME-TYA-PTC			ALL-TYA-PTC		
	N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)
Wave 1	276	71.44 (19.68)	73.22 (57.61 to 89.13)	312	60.79 (18.79)	59.71 (47.52 to 75.00)	193	65.44 (19.07)	66.30 (52.78 to 80.56)
Wave 2	173	77.55 (19.31)	83.70 (61.96 to 93.48)	209	69.46 (19.45)	71.74 (54.35 to 85.87)	122	73.50 (19.08)	77.17 (58.33 to 88.04)
Wave 3	126	79.62 (20.38)	85.87 (68.48 to 95.65)	164	71.33 (18.91)	73.76 (59.75 to 84.78)	99	74.55 (19.26)	80.43 (59.72 to 91.30)
Wave 4	121	78.21 (21.16)	84.78 (64.13 to 95.65)	118	73.30 (33.33)	76.24 (60.87 to 86.96)	98	75.90 (21.27)	82.61 (61.96 to 93.48)
Wave 5	103	80.71 (18.75)	86.96 (71.74 to 95.65)	113	76.21 (18.90)	78.26 (65.22 to 93.48)	75	79.70 (16.78)	85.87 (70.65 to 91.30)

Table A2: Results from adjusted mixed effects models investigating the relationship between levels of TYA care received during the first 12 months from diagnosis and the quality of life – excluding bone cancer (N=667)

		Difference in means	95% Confidence Interval	P-value
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-6.02	-9.02 to -3.02	P=0.0003
	ALL-TYA-PTC	-4.53	-7.72 to -1.35	

* results from a three level model for repeated measurements of QOL over time since diagnosis, with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Table A3: Subgroup investigation for lymphoma v other cancer: Results from adjusted* mixed effects models with interaction terms (N=733)

	TYA care category	Adjusted difference in means	95% confidence interval	P-value from interaction
Cancer type				
Lymphoma	SOME-TYA-PTC v NO-TYA-PTC	-6.01	-9.58 to -2.44	0.90
	ALL-TYA-PTC v NO-TYA-PTC	-4.13	-8.08 to -0.17	
All other cancers	SOME-TYA-PTC v NO-TYA-PTC	-4.89	-9.63 to -0.16	
	ALL-TYA-PTC v NO-TYA-PTC	-4.31	-9.18 to 0.55	

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Table A4: Results from a joint model of longitudinal quality of life scores and survival investigating their relationship with level of TYA care received during the first 12 months from diagnosis (N=733)*

		Difference in means	95% Confidence Interval
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-6.45	-9.34 to -3.56
	ALL-TYA-PTC	-6.11	-9.58 to -2.64

* Models fitted using Stata command *stjm* with a Weibull submodel for survival (reference: M Crowther, K Abrams, P Lambert. Joint modelling of longitudinal and survival data. The Stata Journal (2013) **13**, Number 1, pp. 165–184)Adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis and city (as a fixed effect as a three level model could not be fitted).

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

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	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5 (reference cited for details)
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
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	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	6

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	6, reference cited, also supplemental file
		(b) Give reasons for non-participation at each stage	supplemental file
		(c) Consider use of a flow diagram	supplemental file
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	supplemental file
		(c) Summarise follow-up time (eg, average and total amount)	supplemental file
Outcome data	15*	Report numbers of outcome events or summary measures over time	supplemental file
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	11
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11 and supplemental file
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13-14
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	16

*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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Longitudinal cohort study of the impact of specialist cancer services for teenagers and young adults on quality of life: outcomes from the BRIGHTLIGHT study

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Longitudinal cohort study of the impact of specialist cancer services for teenagers and young adults on quality of life: outcomes from the BRIGHTLIGHT study

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ABSTRACT

Objectives: In England, healthcare policy advocates specialised age-appropriate services for teenagers and young adults (TYA), those aged 13-24 years at diagnosis. Specialist Principal Treatment Centres (PTC) provide enhanced TYA age-specific care, although many still receive care in adult or children's cancer services. We present the first prospective structured analysis of quality of life (QOL) associated with the amount of care received in a TYA-PTC

Design: Longitudinal cohort study

Setting: Hospitals delivering in-patient cancer care in England

Participants: 1,114 young people aged 13-24 years newly diagnosed with cancer

Intervention: Exposure to the TYA-PTC defined as patients receiving NO-TYA-PTC care with those receiving ALL-TYA-PTC and SOME-TYA-PTC care.

Primary outcome: quality of life measured at five time points: 6,12,18, 24 and 36-months after diagnosis

Results: Group mean total QOL improved over time for all patients, but for those receiving NO-TYA-PTC was an average of 5.6 points higher (95% CI 2.8-8.5) than in young people receiving SOME-TYA-PTC care, and 4·2 points higher (95% CI 1.1-7.3) compared to ALL-TYA-PTC care. Differences were greatest 6 months after diagnosis, reduced over time, and did not meet the 8-point level that is proposed to be clinically significant. Young people receiving NO-TYA-PTC care were more likely to have been offered a choice of place of care, be older, from more deprived areas, in work, and have less severe disease. However, analyses adjusting for confounding factors did not explain the differences between TYA groups.

Conclusions: Receipt of some or all care in a TYA-PTC was associated with lower QOL shortly after cancer diagnosis. The NO-TYA-PTC group had higher QOL three years after diagnosis, however those receiving all or some care in a TYA-PTC experienced more rapid QOL improvements. Despite this, the difference were small and may not be clinically significant. Receipt of some care in a TYA-PTC requires further study.

Strengths & limitations of this study

5 bullet points

- We present the first national evaluation of a model of care which aims to improve outcomes for teenagers and young adults with cancer.
- We were able to quantify where young people received care through nationally collated hospital activity data so we could objectively assign young people to a group representing the model of care received.
- Analysis of longitudinal data for three years after diagnosis was adjusted for multiple confounding variables, identified from a conceptual model of patient experience, which underpinned data collection in the study.
- The measure quantifying where care was received was based on the assumption that all teenage and young adult Principal Treatment Centres provided equivalent facilities and care.
- The cohort comprises 20% of young people diagnosed with cancer during the time period, which could impact on the generalisability of the results.

INTRODUCTION

Cancer in teenagers and young adults (TYA) is uncommon. Despite this, cancer in young people aged 15-29 years at diagnosis accounts for an estimated 350,000 new incidence cases and incidence rates are rising[1]. Lower survival rates than younger children in several common cancer types[2] have fuelled many international initiatives aimed to improve outcomes and wellbeing[3,4]. In particular, the need for specialist age-appropriate care and environments are advocated as a critical component of good cancer care for TYA[5-9]. However, the effect on clinical and patient-reported outcomes associated with age-appropriate care are yet to be described[10].

Distinct cancer service provision for TYA began in the United Kingdom (UK) in the 1990s[11]. This was initiated by clinician and patient advocacy, promoting principles which responded to young people's reports of care that frequently lacked support for their priorities of progress towards normal life goals and care alongside others of a similar age delivered by professionals who understood young people[12]. Specialised UK National Health Services (NHS) for young people with cancer have been mandated in England since 2005 by National Institute for Health and Clinical Excellence (NICE) guidance[3]. The guidance identified that young people's needs may be poorly met in children's and older adult services working in isolation from each other[4], and that TYA-specific places of treatment and care may be key to achieving better outcomes for young people with cancer[9] due in part to the distinct impact of cancer on young people's wellbeing, such as in the physical, psychosocial and developmental domains[13].

The delivery of cancer care for TYA in England

Healthcare in England is in the main, publicly funded through the NHS providing universal comprehensive healthcare to all citizens. “The service is configured to improve, prevent, diagnose and treat physical and mental health problems with equal regard”[14]. Secondary care, thus cancer care is delivered in NHS Trusts which oversee NHS hospitals and specialist care centres serving a geographical catchment area[15]’. A Trust may comprise of one or several hospitals, each providing different or similar services, depending on local need. A Trust may comprise of one or several hospitals, each providing different or similar services, depending on local need[15].

The model of specialised TYA cancer care implemented from 2005 focused on 13 TYA Principal Treatment Centres (TYA-PTC) in England. This was to complement the existing services delivered in children’s cancer units (aged up to 16 years in the main but local variation would accept older teenagers) and adult cancer services from 18 years onward. The TYA-PTCs were funded to deliver specialist care, which included the same standard of cancer care as the children and adult units but care was enhanced by the addition of age-appropriate environments and multi-disciplinary teams experienced in working with TYA. For example, providing education and career support to enable TYA to continue with education and employment at a critical time in their lives; nurse specialists who were skilled at discussing challenging subjects (sex, fertility, drug and alcohol use); space to interact with other TYA with cancer to promote normal development and youth support coordinators who provide youth support and facilitate peer to peer activities(see Morgan et al[7] for examples of what is included in a TYA unit).

The location of the TYA-PTCs were chosen based on a number of factors, including existing established service, geographical location and other cancer services available. The guidance directed that TYA aged 16-18 years were treated in a TYA-PTC. The model for young adults aged 19-24 years was to offer choice to receive care in a TYA-PTC or a local cancer unit if it were designated as able to provide their cancer treatment and at least some aspects of age-appropriate care. There was variation in the lower age of admission in TYA-PTCs based on history and availability of other services locally so this resulted in TYA aged 13-16 being treated in a children’s cancer unit or TYA-PTC and those aged 17-24 could be admitted to a TYA-PTC or adult cancer unit. By 2010, about two-thirds of those aged 15-18 years and one-third of 19-24-year olds were believed to have contact with a TYA-PTC[16]. Place of care was therefore directed by clinicians based on cancer type and geographical location. While there is an international mobilisation to implement specialist TYA services[12], including in other European countries, Australasia and North America, the impact of such services on clinical outcomes has not been robustly evaluated.

The BRIGHTLIGHT study is a prospective evaluation of the benefits of specialist TYA services in the English NHS. In order to capture the complexity of the delivery of TYA cancer care, it comprised an evaluation from the perspective of the environment of care [17], the workforce delivering care [18] and young people receiving care. BRIGHTLIGHT was developed with extensive input from young people as well as health professionals [6, 9, 19] and based on consultation with young people[20]. This included input into the selection of the primary outcome: quality of life (QOL).

Quality of Life is defined as "…subjective, multidimensional and dynamic. It is unique to each individual and includes aspects of physical, psychological and social function. It is dependent not only upon the stage of development but also the illness trajectory. This involves the achievement of goals and aspirations and the constraints imposed through ill health and treatment"[21]. Measurement of QOL uses the patient's own report to evaluate the spectrum of impact of illness upon them and has become an increasingly valued healthcare outcome. Previous reports of young people's QOL after a cancer diagnosis have shown this to be significantly lower than normative population data[22]. Longitudinal assessment has indicated QOL improved in the first year after diagnosis but there was no significant improvement in the second year [23]. No evaluation beyond the second year has been reported and while studies have investigated predictors of QOL there has been no evaluation of the impact of different models of delivery of care on QOL. We examined QOL at 6, 12, 18, 24 and 36 months after diagnosis in relation to the proportion of care young people received in a TYA-PTC

METHODS

Study design

The BRIGHTLIGHT study is a mixed methods programme of research. Results from an embedded longitudinal cohort study, obtaining data from young people through a bespoke survey[24], are reported here. The survey was administered at five time points during the first three years after diagnosis (6, 12, 18, 24 and 36 months, waves 1-5 respectively). A scale was developed, previously described in detail[25], using Hospital Episode Statistics (HES) in-patient data to measure episodes of care in different NHS Trusts and then used to assign young people to one of three levels of TYA care dependent on how much in-patient HES activity recorded in the first 12 months after diagnosis was delivered in a TYA-PTC: no care in a TYA-PTC, i.e., all care was delivered in a children's or adult cancer unit (NO-TYA-PTC), some care delivered in a TYA-PTC with additional care in a children's or adult cancer unit (SOME-TYA-PTC) or all care delivered in a TYA-PTC (ALL-TYA-PTC).

Patient and public involvement

BRIGHTLIGHT has been developed with young people from the point of inception and our Young Advisory Panel (YAP) have been involved in the management, implementation and dissemination of the study. This has been reported in detail previously [20, 26-29] but in summary, BRIGHTLIGHT was developed based on consultation with young people attending a patient conference in 2008: place of care was identified as the third priority for future research. Young people worked with the research team to conduct the research informing the National Institute for Health Research grant application[6] including representation as a co-applicant. The YAP have advised on changes to recruitment[28], helped develop the retention strategy[26], informed additional studies[29], and are involved in dissemination[30].

Participants and setting

BRIGHTLIGHT was open to recruitment between October 2012 and April 2015 in 109 English NHS hospitals of which 97 recruited at least one young person. Eligibility was defined as aged 13-24 years at the time of diagnosis, newly diagnosed with cancer (ICD-10

codes C00-C97) and recruited within four months of diagnosis. There was no eligibility exclusion for a language or sensory impairment affecting communication. The following groups were excluded: those serving a custodial sentence; not anticipated to be alive at the first point of data collection (6-months after diagnosis); or incapable of completing a survey. Details of the recruitment process are reported elsewhere[25,31]. Young people gave written consent and parental consent was also obtained for those less than 16 years. Checks were made through the Demographic Batch Service at NHS digital before each wave of data collection to ensure young people were alive and to obtain their most recent address. The study was approved by London-Bloomsbury NHS Research Ethics Committee and the Confidentiality Advisory Group of the Health Research Authority.

The sample size calculation was based on a comparison between the three levels of TYA care[25] for the primary outcome of PedsQL total score[32], measured at five time points over the three-year follow-up. Previously reported PedsQL data for childhood cancer patients suggested a standard deviation for this score of 16[33]. To detect a difference in scores of 8 units with 80% power[34] required a sample of 200 young people. This calculation assumed a significance level of 0.01 (2 sided) to allow for multiple comparisons between three levels of TYA care and assumed an average of three repeated measurements per patient (intra cluster correlation 0.3 as suggested as a maximum for similar patient outcomes[35]). The calculation allowed for adjustment for confounding factors using a variance inflation factor with a correlation of 0.5[36]. To ensure adequate power to examine the effect of TYA care on QOL within subgroups of age at diagnosis (13-18 and 19-24 years) and type of tumour (haematological, solid tumour groups), the minimum required sample size was raised to 800 (80% power).

Data collection

Data were collected from three sources: young people's self-report, patient clinical records, and NHS and Public Health England (PHE) databases. Details of these data sources are reported elsewhere[25]. Data presented here are responses to the BRIGHTLIGHT Survey, a bespoke survey containing five validated questionnaires and 169 descriptive questions related to post diagnosis experience. The survey was administered through face-to-face interviews in young people's homes by an independent research company at the first time point and either online or telephone interview at subsequent waves of data collection[24].

This paper reports data for the primary outcome, QOL, which was measured using the Pediatric Quality of Life Questionnaire (PedsQL)[32]. At the time of study development this was the only measure of QOL validated for teenagers and young adults[37]. It contains 23 items rated using a five-point Likert Scale (Never, Almost never, Sometimes, Often, Almost always). Responses are presented as four domain scores (physical, emotional, social, and work/studies functioning), two summary scores (physical and psychosocial function) and a total score. Domain, summary and total scores range from 0-100, with 100 representing the best possible QOL.

Analysis

Analysis was carried out following a predefined statistical analysis plan using STATA version 15. A mixed effects model was used to investigate the relationship between the levels of TYA care and the PedsQL total score, allowing for repeated measurements taken over the 3 years since diagnosis. The model was adjusted for confounding factors identified based on

the conceptual model underpinning the BRIGHTLIGHT Survey[6,24] and using a causal diagram in the form of a Directed Acyclic Graph (DAG) (DAGitty software www.dagitty.net; Supplemental File, Figure A1). Factors adjusted for were age at diagnosis, type of cancer (leukaemia, lymphoma, brain and central nervous system, bone tumours, sarcoma, germ cell, melanoma, carcinomas, other), socioeconomic status (Index of Multiple Deprivation (IMD)[38] quintile), severity of cancer (least, intermediate, most[25]), ethnicity (white, other), choice offered about where to receive treatment (yes/no), presence of any long term condition prior to cancer (yes/no), days from first symptom to diagnosis and number of General Practitioner visits before diagnosis. Geographical location (specified as 12 cities, derived from the TYA-PTC and their network of hospitals) was included in the model as a random effect. Models were extended to include interaction terms to investigate predefined subgroup effects by age at diagnosis (both as a continuous factor and using categories of 13-18 and 19-24 years) and tumour type (haematological and solid tumours). An interaction with time since diagnosis was also examined to investigate whether the relationship between level of TYA care and QOL changed over time. Similar models were fitted for the PedsQL domain scores for physical, social, emotional and work/school/college functioning, and the psychosocial summary score.

The extent and patterns of missing QOL data over time were examined using summary statistics and profile plots. As there is no provision in the scoring of PedsQL to directly account for death, our main analysis did not distinguish between data 'missing' following death and that missing for other reasons. With the possibility of informative missing data due to deaths, a sensitivity analysis was carried where joint mixed-effect models for the longitudinal QOL scores and time until death were fitted to account for the correlation between the QOL and survival outcomes[39]. The QOL estimates for the effect of level of TYA care were then compared with those obtained from previously fitted mixed models.

RESULTS

A total of 1,126 young people were recruited. BRIGHTLIGHT survey data at wave 1 were available for 830 (75%) participants and details of numbers at each wave are summarised in Figure 1. Characteristics of those who did and did not complete wave 1 were similar, except for a higher proportion of non-white participants not completing wave 1 (12% vs. 19%, p=.004) [25]. Forty-eight participants could not be assigned a level of TYA-PTC care as there were no linked HES inpatient records available. Data from 782 young people were therefore included. There were fewer young people receiving ALL-TYA-PTC care (n=193; 25%) in comparison to SOME-TYA-PTC (n=312; 40%) and NO-TYA-PTC (n=277; 35%). Demographic characteristics and summary of variables adjusted for in the analysis are shown in Table 1. Young people who received NO-TYA-PTC care were slightly older, more likely to be working full/part time, had less severe disease, had a better prognosis and were more likely to have been given a choice in their place of care. Young people who had ALL-TYA-PTC care were more likely to come from less deprived areas.

Table 1: Participant characteristics according to level of care at wave 1

Characteristic		Level of TYA care at 12 months from diagnosis		
		NO-TYA-PTC N=277	**SOME-TYA-PTC N=312**	**ALL-TYA-PTC N=193**
Age at diagnosis (years)	Mean (SD)	21·04 (3.01)	19·40 (3.41)	19·97 (3.15)
Age groups	13-15 years 16-18 years 19-24 years	37 (10%) 34 (10%) 288 (80%)	72 (17%) 128 (31%) 215 (52%)	40 (15%) 78 (29%) 152 (56%)
Gender	Male Female	148 (53%) 129 (47%)	165 (53%) 147 (47%)	112 (58%) 81 (42%)
Ethnicity*	White Mixed Asian Black Other	252 (91%) 4 (1%) 15 (5%) 4 (1%) 2 (1%)	273 (88%) 5 (2%) 24 (8%) 7 (2%) 3 (1%)	163 (84%) 4 (2%) 20 (10%) 2 (1%) 4 (2%)
Socioeconomic status (IMD quintile)	1 – most deprived 2 3 4 5 – least deprived	66 (24%) 47 (17%) 51 (19%) 65 (24%) 46 (17%)	73 (24%) 52 (17%) 60 (20%) 61 (20%) 59 (19%)	34 (18%) 32 (17%) 37 (20%) 40 (21%) 46 (24%)
Marital Status	Married/civil partnership Cohabiting Single/divorced	9 (4%) 43 (17%) 198 (79%)	8 (3%) 27 (10%) 227 (87%)	6 (3%) 18 (10%) 148 (86%)
Current status	Working full/part time In education Other work (apprentice/intern/voluntary)	126 (45%) 61 (22%) 6 (2%)	72 (23%) 112 (36%) 5 (2%)	43 (22%) 81 (42%) 6 (3%)

	Unemployed	10 (4%)	11 (4%)	7 (4%)
	Long term sick	39 (14%)	51 (16%)	31 (16%)
	Not seeking work	35 (13%)	61 (20%)	25 (13%)
Type of cancer (Birch classification)				
	Leukaemia	19 (7%)	49 (16%)	33 (17%)
	Lymphoma	111 (40%)	75 (24%)	70 (36%)
	CNS	9 (3%)	9 (3%)	12 (6%)
	Bone	7 (3%)	59 (19%)	3 (2%)
	Sarcomas	8 (3%)	31 (10%)	15 (8%)
	Germ cell	64 (19%)	55 (18%)	31 (16%)
	Skin	22 (8%)	1 (<1%)	4 (2%)
	Carcinomas (not skin)	41 (15%)	31 (10%)	23 (12%)
	Miscellaneous specified**	5 (2%)	2 (<1%)	1 (<1%)
	Unspecified Malignant	1 (<1%)	0	1 (<1%)
Severity at diagnosis (row %, column %)				
	Least	200 (46%, 72%)	133 (31%, 43%)	95 (22%, 49%)
	Intermediate	49 (26%, 18%)	82 (44%, 26%)	56 (30%, 29%)
	Most	28 (17%, 10%)	97 (58%, 31%)	42 (25%, 22%)
Prognostic score				
	<50%	21 (8%)	60 (19%)	41 (21%)
	50-80%	54 (20%)	125 (40%)	44 (23%)
	>80%	200 (73%)	126 (41%)	108 (56%)
Location* **				
	Birmingham	41 (15%)	59 (19%)	12 (6%)
	Bristol	51 (18%)	32 (10%)	4 (2%)
	Cambridge	12 (4%)	8 (3%)	1 (1%)
	Manchester	22 (8%)	35 (11%)	11 (6%)
	Merseyside	13 (5%)	11 (4%)	6 (3%)
	East Midlands	15 (5%)	24 (8%)	60 (31%)
	Leeds	20 (7%)	25 (8%)	25 (13%)
	Newcastle	13 (5%)	6 (2%)	24 (12%)
	Oxford	5 (2%)	4 (1%)	7 (4%)

	London Sheffield Southampton	60 (22%) 7 (3%) 18 (7%)	83 (27%) 9 (3%) 16 (5%)	10 (5%) 9 (5%) 24 (12%)
Given a choice about where to receive treatment[$]	 Yes No (or < 19 years)	N=272 121 (45%) 151 (56%)	N=311 86 (28%) 225 (72%)	N=192 48 (25%) 144 (75%)
Long term condition prior to cancer	 Yes No	N=277 20 (7%) 257 (93%)	N=311 34 (11%) 277 (89%)	N=193 18 (9%) 175 (91%)
Time to diagnosis: days from 1st symptom	Median (IQR), [min, max]	N=264 62 (29·5 to 168·5) [0, 1340]	N=304 65·5 (29·5 to 152·5) [0, 959]	N=188 63·5 (25·5 to 151·0) [0, 1217]
Time to diagnosis: number of GP visits before diagnosis	Median (IQR), [min, max]	N=274 1 (0 to 3) [0, 20]	N=311 1 (0 to 3) [0, 20]	N=193 2 (1 to 3) [0, 40]

* Wave 1 data was used with missing values completed using available PHE data.

** includes 4 'unclassified' – treated in cancer unit but did not have cancer

***Includes the TYA-PTC and hospitals linked to the multi-disciplinary team at the TYA-PTC; where available based on hospital of diagnosis, for 77 cases based on recruiting hospital

$ Those <19 years at diagnosis were assumed not to have been given a choice

Longitudinal changes in the average QOL total score according to the level of care are shown in Figure 2 (summary by wave is given in Supplemental file, Table A1). Across all time periods this illustrates lower QOL score for those in the SOME and ALL-TYA-PTC groups compared to the NO-TYA-PTC group. Differences between level of care appeared to diminish steadily over time. The negative coefficients for levels of care from the model indicate that across the 3 year period of the study QOL scores were on average higher for those with NO-TYA-PTC care compared with SOME-TYA-PTC and ALL-TYA-PTC with a larger difference compared with the SOME-TYA-PTC category (Table 2). The differences were statistically significant but fell inside the threshold of 8 points proposed to be clinically significant [32]. There was no evidence that the relationship between QOL and level of care was different for the combined group of leukaemia/lymphomas compared with other cancers. Also, there was no evidence of a difference by age at diagnosis (Figure 3). There was evidence that the QOL/Level of care relationship changed over time such that differences between the groups diminished i.e. slopes for SOME-TYA-PTC and ALL-TYA-PTC over time are steeper than for NO-TYA-PTC, therefore rates of improvement of QOL were superior in the ALL-TYA-PTC and SOME-TYA-PTC (Table 3), mirroring what was seen in Figure 2.

Analysis of the physical functioning and work/school/college functioning domain scores showed a similar pattern to that seen for the total QOL score. The SOME-TYA-PTC group had a mean difference in physical functioning of -8.28 compared to the NO_TYA-PTC group, which was statistically significant and above the threshold for clinical significance. For the emotional functioning domain however, difference between groups were less marked and notably the average difference in scores between the SOME-TYA-PTC and NO-TYA-PTC was reduced. Difference between groups in terms of social functioning and the psychosocial summary scores were small and not statistically significant (Figures 4-8, Table 2).

Table 2: Mixed model investigating the relationship between levels of TYA care received during the first 12 months from diagnosis and total quality of life and domain scores over 3 years (N=733)

		Difference in means	95% Confidence Interval	P-value
TOTAL QUALITY OF LIFE SCORE (n=733)				
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-5.63	-8.49 to -2.77	P=0.0005
	ALL-TYA-PTC	-4.17	-7.28 to -1.07	
PHYSICAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-8.28	-11.95 to -4.61	P=0.0001
	ALL-TYA-PTC	-4.79	-8.76 to -0.81	
EMOTIONAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-4.29	-7.79 to -0.80	P=0.015
	ALL-TYA-PTC	-5.43	-9.29 to -1.57	
SOCIAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-2.96	-5.77 to -0.16	P=0·099
	ALL-TYA-PTC	-2.49	-5.60 to 0.62	
WORK/SCHOOL/COLLEGE FUNCTIONING (N=595)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-6.87	-10.45 to -3.30	P=0.0007
	ALL-TYA-PTC	-4.67	-8.47 to -0.87	
PSYCHOSOCIAL SUMMARY SCORE (N=600)				
TYA care category	**SOME-TYA-PTC**	-2.51	-5.71 to 0.70	P=0.074

(v NO-TYA-PTC)	**ALL-TYA-PTC**	-3.96	-7.44 to -0.48	

* results from a three level model for repeated measurements of QOL over time since diagnosis, with a random effect for geography and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis. Missing data for 96 due to missing TYA category and missing data in other covariates
** Likelihood ratio test

Table 3: Investigation of changes in QOL score over time: Results from adjusted* mixed effects models with interaction term (time months x TYA-PTC category). Coefficients for time describe the linear increase in QOL score per month within each TYA care category (N=733)

TYA care category	Coefficient for time (per month)	95% confidence interval	P-value from interaction
NO-TYA-PTC	0·26	0·18 to 0·34	0·004
SOME-TYA-PTC	0·45	0·37 to 0·53	
ALL-TYA-PTC	0·37	0·27 to 0·46	

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Results from post hoc analysis excluding patients with bone tumours were similar to those for all cancers combined (Supplemental file, Table A2). A subgroup investigation of patients with lymphoma, the biggest diagnostic category, showed these were not significantly different from those for the group of other cancer types (Supplemental file, Table A3). Finally, sensitivity analyses using joint modelling for survival alongside longitudinal QOL did not alter the conclusion based on the main results (Supplemental file, Table A4).

DISCUSSION

Our study is the first reported national longitudinal evaluation of specialist cancer services, more specifically TYA-PTCs and their networks of care, as they were originally defined in 2005[3]. We recorded patient outcomes to determine the influence of place of care, and after consultation with patients and professionals, selected QOL as the primary parameter of interest. Using routinely collected hospital admission data to identify time spent in the TYA-PTC, we categorised patients by the level of their care received in the TYA-PTC (all, none or some). We found that there was a statistically significant difference between these groups with those in the NO-TYA-PTC group having superior QOL compared to those in the ALL-TYA-PTC group, whilst those in the SOME-TYA-PTC group reported lowest QOL. Quality of life improved over time in all three groups, but rates of improvement were significantly better for SOME and ALL-TYA-PTC.

We predicted that sociodemographic or disease factors might explain some of the differences between groups and adjusted the analyses for these confounding variables. Despite extensive analysis we were unable to identify other factors to account for these differences. Like other reports of young people's QOL after a cancer diagnosis[22], we found this to be low, irrespective of where young people were treated. We found that young people who did not access a TYA-PTC had better QOL in comparison to those who had all or some of their care in a TYA-PTC. However, while this was statistically significant, the mean

difference between the NO-TYA-PTC and ALL-TYA-PTC groups was not at a level proposed as clinically significant (8-point difference[33]). Nevertheless, it is important to consider reasons for lower QOL when young people experience multiple types of place of care and the determinants of place of care. Based on work in other settings where care is delivered on multiple sites [40] we surmise that this may result from limited coordination of care, perhaps including inadequate communication with and between professionals. Having to repeat conversations and explanations of their cancer diagnosis and treatment details is frequently reported as burdensome to young people[6]. A greater understanding of the determinants of place of care for young people and the factors which influence a sense of care co-ordination deserve further exploration.

It is interesting that young people who had no access to the TYA-PTC rated their QOL the highest. This could reflect young people rating themselves by comparison with the other people they could see being treated for cancer outside of a TYA-PTC, including older adults. It could also be that young people chose to receive care locally rather than travel to the TYA-PTC so they could keep their links to their 'normal' life, which is supported by the domain level analysis where they also rated their work/school/college functioning higher. Alternatively, the strong emphasis placed on the unique issues faced by TYA with cancer by members of the TYA MDT staff may have heightened patients' awareness of these problems in comparison to the NO-TYA-PTC group, and consequently they lowered their perception of their QOL while the NO-TYA-PTC group remained comparatively unaware of such concerns. Future work could focus on the influence of being given a choice in the place where young people receive care, and the factors that young people consider to be important when making this decision.

The longest follow-up for longitudinal assessment of QOL previously reported to two years after diagnosis[23], which showed no improvement after the first year. However, we found that there was a gradual improvement in QOL over 3-years, which was more rapid when young people received all their care in a TYA-PTC. The philosophy of TYA cancer care includes the delivery of care to support young people to achieve their long-term personal outcomes (education, employment and relationships), the benefits of care provided by the TYA-PTC may therefore not be realised in the short-term. It would be beneficial for us to understand whether this improvement continued into long-term survivorship, especially the influence of QOL reaching and sustaining goals such as employment.

There are several limitations to this study including how specialist care was defined and measured. This was based on the location of the 13 NHS Trusts in England commissioned as TYA-PTCs but not the specific hospitals within these Trusts where the specialist TYA services were based. For example, a Trust which included multiple hospitals could only have specialist TYA services in one therefore a young person receiving care in one of the other hospitals was assumed to have had access to specialist TYA services, i.e., they were assigned to the ALL-TYA-PTC group rather than NO-TYA-PTC. Furthermore, using the Trust commissioned as a TYA-PTC does not capture the details of the TYA-specific care available or delivered and assumes that this is equal in all. We know there was wide variation in the delivery of care through the duration of the study[41]. However, at the time of study inception HES was the sole data source available that would allow an objective measurement of place of care. In complementary work, the key elements of specialist age-appropriate care for TYA

have been described[17]. This would provide an alternative categorisation against which to measure patient and clinical outcomes.

The cohort represented approximately a fifth of the total cancer population diagnosed between July 2012 and December 2014 as ascertained through the National Cancer Registration and Analysis Service, and there were differences in cancer types between the cohort and those not recruited[25], which could impact on the generalisability of the results. For example, the cohort included a higher proportion of young people with germ cell tumours and lymphoma, but a lower proportion of carcinoma and skin cancers. We used a single mode of survey administration at wave 1, and multiple modes at waves 2-5. While this may have introduced a social desirability bias (noted to be more so for telephone interviews than web-based surveys[42]), this was to increase the response rate as work during the feasibility study for BRIGHTLIGHT indicated no one method was acceptable to all young people. Finally, we used a measure of QOL that was validated across the age 13-24 years[37], but this may not reflect the issues that were most relevant to young people with cancer in the UK (having been developed in the US in a non-cancer population). This is supported by comments made in the cognitive interviews undertaken when the survey was being developed; young people did not agree with the wording of the school functioning domain, so this was changed to work/school/college[24]. However, young people who were not in education, employment or training would not be able to answer these questions. Future work is required to develop TYA-specific QOL measures that reflect issues specific to this population.

Despite these limitations this is the first systematic prospective evaluation of specialist services for young people with cancer. We have found that TYA cancer care as commissioned in 2010 resulted in young people's QOL gradually improving 3-years after diagnosis and improving more rapidly from a lower baseline if young people's treatment involved a TYA-PTC. NHS care pathways may result in care in specialist centres for young people with the poorest initial QOL, and local care for those with the least poor initial QOL, risk stratifying the patients appropriately. Young people who receive some care in both a children's or adult cancer unit and at a TYA-PTC also have an improvement in QOL, but the rate of improvement was less and QOL remained lower than for young people treated in a single type of organisation. The factors influencing place of care and the differences in QOL and survival remain unclear. A model of 'joint care', increasing the emphasis and investment in communication between TYA-PTCs and other Trusts designated to deliver elements of TYA cancer care, is currently proposed by the NHS in England. The influence of such changes in care provision should be examined prospectively in future to identify if QOL of young people with cancer is improved wherever care is received.

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Author contributions:
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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Competing interests:
None declared.

Ethics Approval:
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Data sharing statement:
Further details of the BRIGHTLIGHT programme of work are 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 2020 when the primary analysis is complete. We welcome collaboration, for general data sharing enquiries please contact RMT (rtaylor13@nhs.net).

Figure legends

Figure 1: Participation at each wave of data collection

*Drop-outs between waves due to death, permanent optout 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 2: Mean PedsQL total score over time since diagnosis (with 95% confidence intervals)

Graph based on data collected in Waves 1 to 5, plotted against median time since diagnosis.

Figure 3: Subgroup investigations for cancer type (leukaemia/lymphoma v other) and age group (<19 v 19+): Results from adjusted* random effects models with interaction terms (N=733)

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, Choice about where to receive treatment, Long term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Figure 4: Mean PedsQL physical functioning domain scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 5: Mean PedsQL emotional functioning domain scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 6: Mean PedsQL social functioning domain scores over time since diagnosis (with 95% confidence intervals)

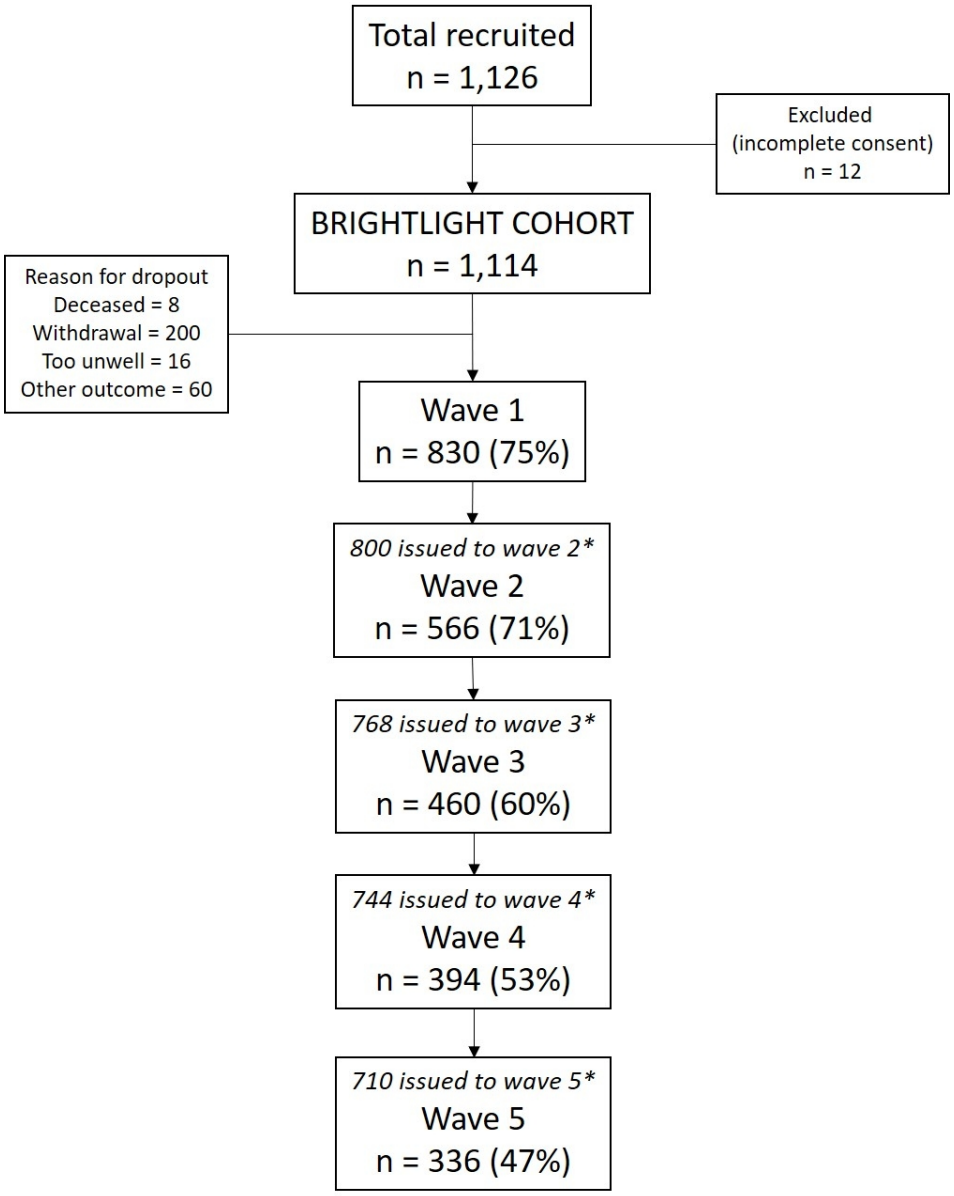
(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 7: Mean PedsQL work/school/college functioning domain scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 8: Mean PedsQL Psychosocial summary score scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)



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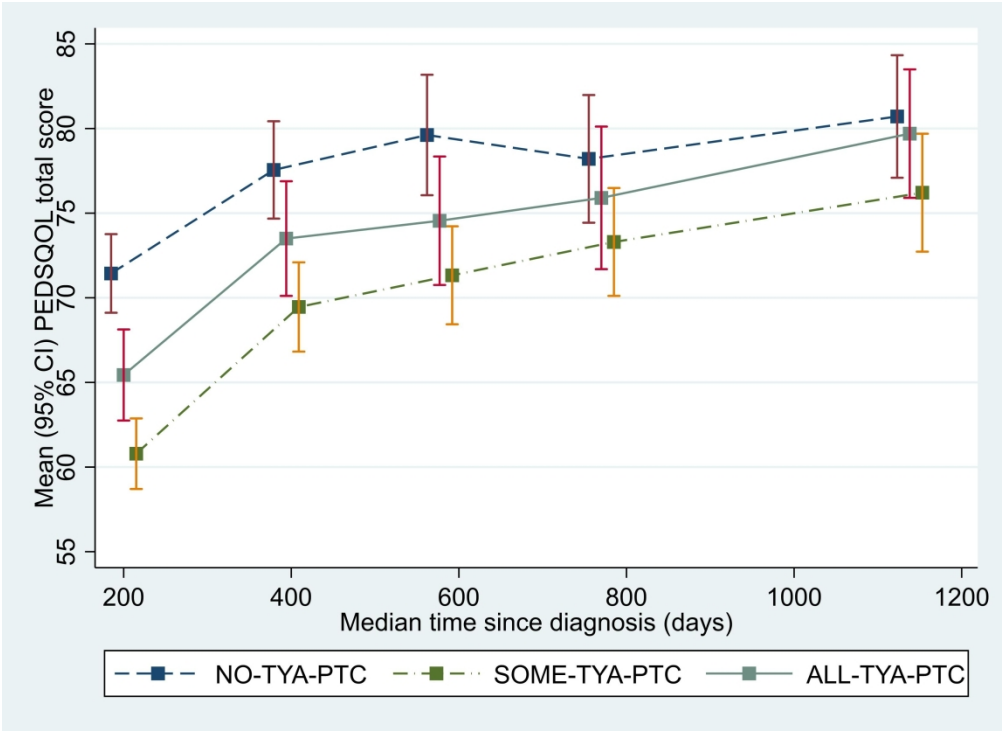

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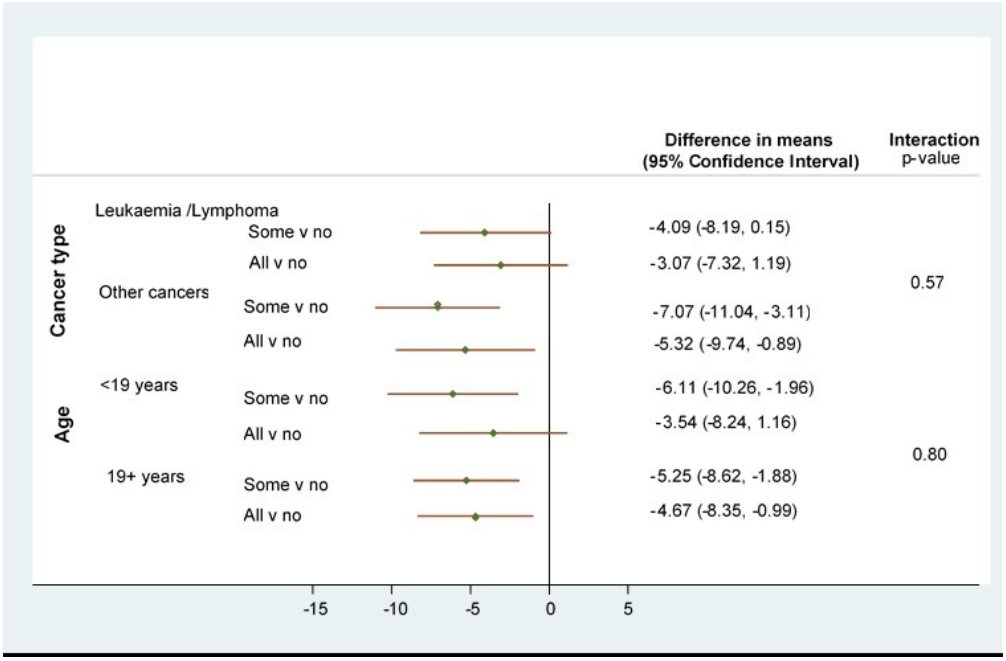

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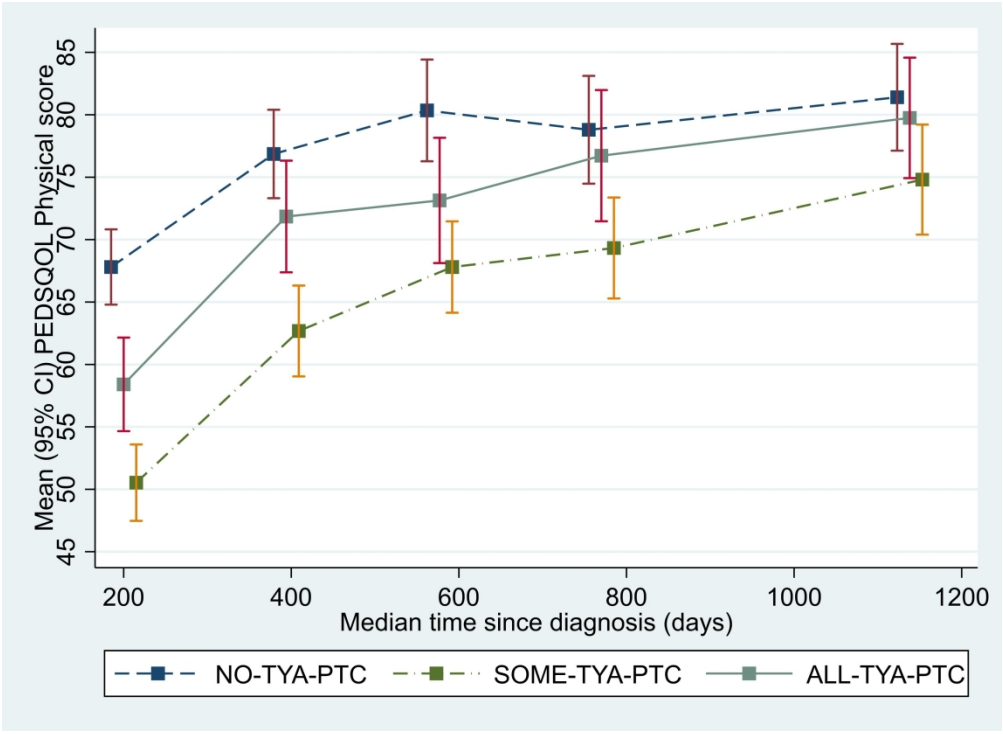

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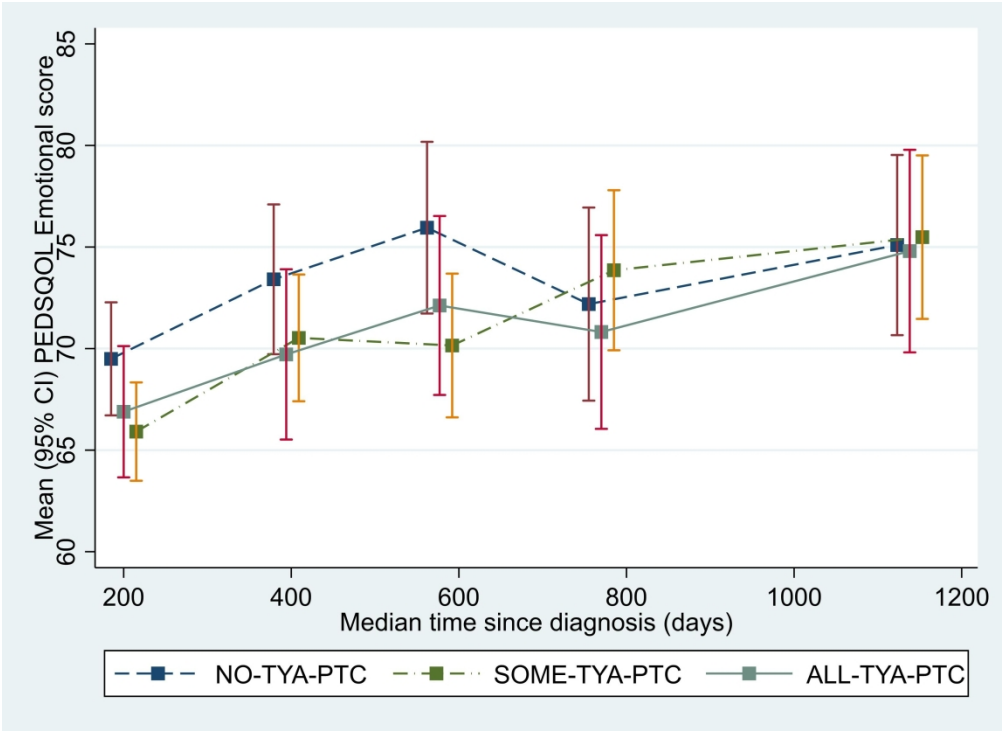

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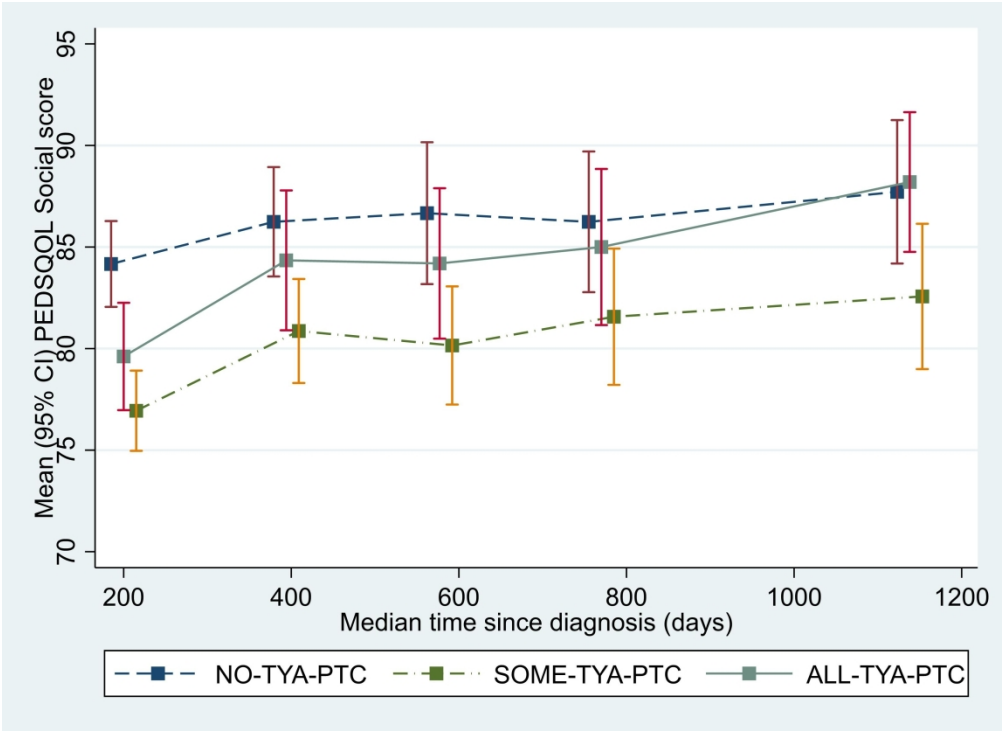

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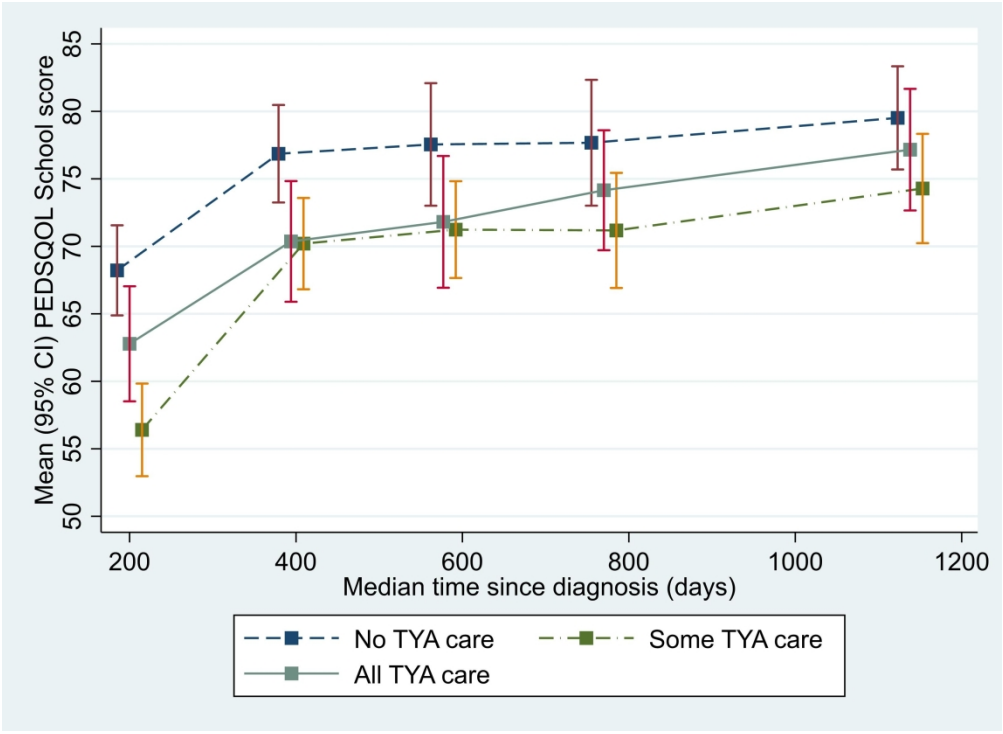

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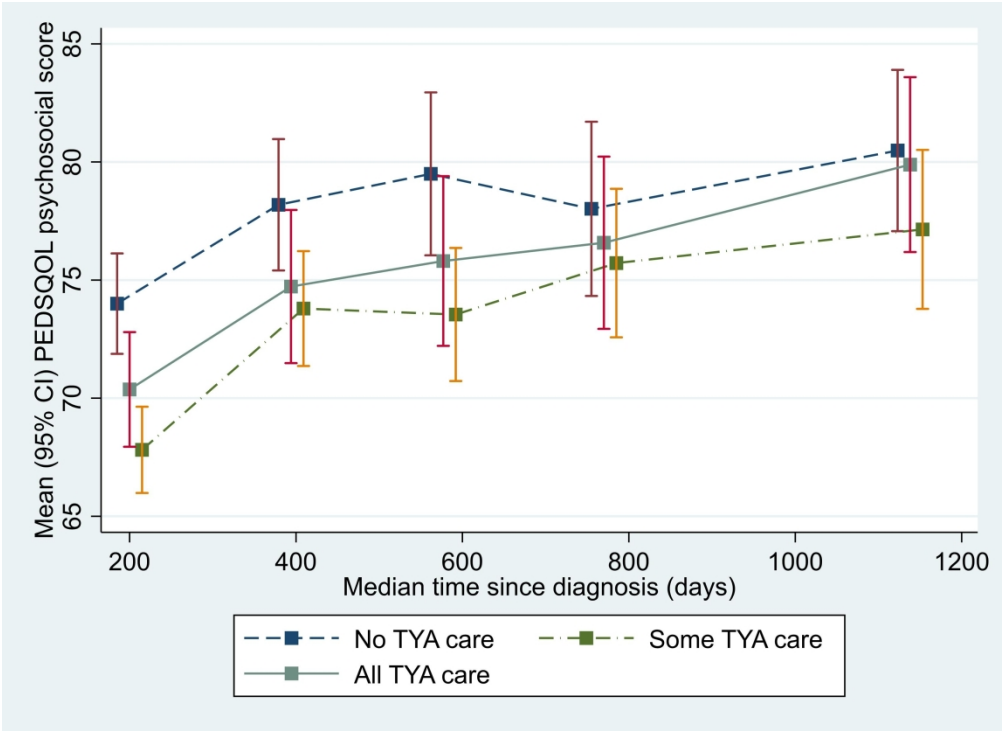

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Supplemental file

Figure A1: Matrix representing the causal diagram explaining confounding variable to enter in the Directed Acyclic Graph (DAG)

	TYA SCL	QOL	Age	Choice	CS	CT	DoH	Ethnicity	Finances	Gender	Geography	I&C	LTC	RtD	SE	SES	SS	Treat-ment
TYA SCL		↗	↗	↗	↗	↗	↗	↗	↗	O	↗	↗	↗	↗	↗	↗	↗	↗
QOL			↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗
Age				↗	O	↗	↗	O	↗	O	O	↗	↗	↗	↗	↗	↗	↗
Choice					↗	↗	O	↗	↗	O	↗	↗	↗	↗	↗	↗	↗	↗
CS						↗	↗	↗	↗	O	↗	↗	↗	↗	↗	↗	↗	↗
CT							↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗
DoH								↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗
Ethnicity									↗	O	↗	↗	↗	↗	↗	↗	↗	↗
Finances										O	↗	↗	↗	↗	O	↗	↗	↗
Gender											O	↗	↗	↗	↗	O	↗	↗
Geography												↗	↗	↗	↗	↗	↗	↗
I&C													↗	↗	↗	↗	↗	↗
LTC														↗	↗	↗	↗	↗
RtD															↗	↗	↗	↗
SE																↗	↗	↗
SES																	↗	↗
SS																		↗
Treatment																		

CS: cancer severity; CT: cancer type; DoH: duration of hospitalisation; I&C: information & communication; LTC: long-term condition; QOL: quality of life; RtD: route to diagnosis; SE: symptom experience; SES: socioeconomic status; SS: social support

O – indicates a null relationship

Table A1: PedsQL total score by Wave of data collection

	NO-TYA-PTC			SOME-TYA-PTC			ALL-TYA-PTC		
	N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)
Wave 1	276	71.44 (19.68)	73.22 (57.61 to 89.13)	312	60.79 (18.79)	59.71 (47.52 to 75.00)	193	65.44 (19.07)	66.30 (52.78 to 80.56)
Wave 2	173	77.55 (19.31)	83.70 (61.96 to 93.48)	209	69.46 (19.45)	71.74 (54.35 to 85.87)	122	73.50 (19.08)	77.17 (58.33 to 88.04)
Wave 3	126	79.62 (20.38)	85.87 (68.48 to 95.65)	164	71.33 (18.91)	73.76 (59.75 to 84.78)	99	74.55 (19.26)	80.43 (59.72 to 91.30)
Wave 4	121	78.21 (21.16)	84.78 (64.13 to 95.65)	118	73.30 (33.33)	76.24 (60.87 to 86.96)	98	75.90 (21.27)	82.61 (61.96 to 93.48)
Wave 5	103	80.71 (18.75)	86.96 (71.74 to 95.65)	113	76.21 (18.90)	78.26 (65.22 to 93.48)	75	79.70 (16.78)	85.87 (70.65 to 91.30)

Table A2: Results from adjusted mixed effects models investigating the relationship between levels of TYA care received during the first 12 months from diagnosis and the quality of life – excluding bone cancer (N=667)

		Difference in means	95% Confidence Interval	P-value
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-6.02	-9.02 to -3.02	P=0.0003
	ALL-TYA-PTC	-4.53	-7.72 to -1.35	

* results from a three level model for repeated measurements of QOL over time since diagnosis, with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Table A3: Subgroup investigation for lymphoma v other cancer: Results from adjusted* mixed effects models with interaction terms (N=733)

	TYA care category	Adjusted difference in means	95% confidence interval	P-value from interaction
Cancer type				
Lymphoma	SOME-TYA-PTC v NO-TYA-PTC	-6.01	-9.58 to -2.44	0.90
	ALL-TYA-PTC v NO-TYA-PTC	-4.13	-8.08 to -0.17	
All other cancers	SOME-TYA-PTC v NO-TYA-PTC	-4.89	-9.63 to -0.16	
	ALL-TYA-PTC v NO-TYA-PTC	-4.31	-9.18 to 0.55	

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Table A4: Results from a joint model of longitudinal quality of life scores and survival investigating their relationship with level of TYA care received during the first 12 months from diagnosis (N=733)*

		Difference in means	95% Confidence Interval
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-6.45	-9.34 to -3.56
	ALL-TYA-PTC	-6.11	-9.58 to -2.64

* Models fitted using Stata command *stjm* with a Weibull submodel for survival (reference: M Crowther, K Abrams, P Lambert. Joint modelling of longitudinal and survival data. The Stata Journal (2013) **13**, Number 1, pp. 165–184)Adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis and city (as a fixed effect as a three level model could not be fitted).

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

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	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5 (reference cited for details)
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
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	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	6

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	6, reference cited, also supplemental file
		(b) Give reasons for non-participation at each stage	supplemental file
		(c) Consider use of a flow diagram	supplemental file
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	supplemental file
		(c) Summarise follow-up time (eg, average and total amount)	supplemental file
Outcome data	15*	Report numbers of outcome events or summary measures over time	supplemental file
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	11
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11 and supplemental file
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13-14
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	16

*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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Longitudinal cohort study of the impact of specialist cancer services for teenagers and young adults on quality of life: outcomes from the BRIGHTLIGHT study

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Longitudinal cohort study of the impact of specialist cancer services for teenagers and young adults on quality of life: outcomes from the BRIGHTLIGHT study

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Keywords: BRIGHTLIGHT, teenagers and young adults, cancer, observational research, cohort, outcome, quality of life, experience

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ABSTRACT

Objectives: In England, healthcare policy advocates specialised age-appropriate services for teenagers and young adults (TYA), those aged 13-24 years at diagnosis. Specialist Principal Treatment Centres (PTC) provide enhanced TYA age-specific care, although many still receive care in adult or children's cancer services. We present the first prospective structured analysis of quality of life (QOL) associated with the amount of care received in a TYA-PTC

Design: Longitudinal cohort study

Setting: Hospitals delivering in-patient cancer care in England

Participants: 1,114 young people aged 13-24 years newly diagnosed with cancer

Intervention: Exposure to the TYA-PTC defined as patients receiving NO-TYA-PTC care with those receiving ALL-TYA-PTC and SOME-TYA-PTC care.

Primary outcome: quality of life measured at five time points: 6,12,18, 24 and 36-months after diagnosis

Results: Group mean total QOL improved over time for all patients, but for those receiving NO-TYA-PTC was an average of 5.6 points higher (95% CI 2.8-8.5) than in young people receiving SOME-TYA-PTC care, and 4·2 points higher (95% CI 1.1-7.3) compared to ALL-TYA-PTC care. Differences were greatest 6 months after diagnosis, reduced over time, and did not meet the 8-point level that is proposed to be clinically significant. Young people receiving NO-TYA-PTC care were more likely to have been offered a choice of place of care, be older, from more deprived areas, in work, and have less severe disease. However, analyses adjusting for confounding factors did not explain the differences between TYA groups.

Conclusions: Receipt of some or all care in a TYA-PTC was associated with lower QOL shortly after cancer diagnosis. The NO-TYA-PTC group had higher QOL three years after diagnosis, however those receiving all or some care in a TYA-PTC experienced more rapid QOL improvements. Despite this, the difference were small and may not be clinically significant. Receipt of some care in a TYA-PTC requires further study.

Strengths & limitations of this study

5 bullet points

- We present the first national evaluation of a model of care which aims to improve outcomes for teenagers and young adults with cancer.
- We were able to quantify where young people received care through nationally collated hospital activity data so we could objectively assign young people to a group representing the model of care received.
- Analysis of longitudinal data for three years after diagnosis was adjusted for multiple confounding variables, identified from a conceptual model of patient experience, which underpinned data collection in the study.
- The measure quantifying where care was received was based on the assumption that all teenage and young adult Principal Treatment Centres provided equivalent facilities and care.
- The cohort comprises 20% of young people diagnosed with cancer during the time period, which could impact on the generalisability of the results.

INTRODUCTION

Cancer in teenagers and young adults (TYA) is uncommon. Despite this, cancer in young people aged 15-29 years at diagnosis accounts for an estimated 350,000 new incidence cases and incidence rates are rising[1]. Lower survival rates than younger children in several common cancer types[2] have fuelled many international initiatives aimed to improve outcomes and wellbeing[3,4]. In particular, the need for specialist age-appropriate care and environments are advocated as a critical component of good cancer care for TYA[5-9]. However, the effect on clinical and patient-reported outcomes associated with age-appropriate care are yet to be described[10].

Distinct cancer service provision for TYA began in the United Kingdom (UK) in the 1990s[11]. This was initiated by clinician and patient advocacy, promoting principles which responded to young people's reports of care that frequently lacked support for their priorities of progress towards normal life goals and care alongside others of a similar age delivered by professionals who understood young people[12]. Specialised services for young people being treated for cancer within the National Health Service (NHS) have been mandated in England since 2005 by the National Institute for Health and Clinical Excellence (NICE) guidance[3]. The guidance identified that young people's needs may be poorly met in children's and older adult services working in isolation from each other[4], and that TYA-specific places of treatment and care may be key to achieving better outcomes for young people with cancer[9] due in part to the distinct impact of cancer on young people's wellbeing, such as in the physical, psychosocial and developmental domains[13].

The delivery of cancer care for TYA in England

Healthcare in England is in the main, publicly funded through the NHS providing universal comprehensive healthcare to all citizens. “The service is configured to improve, prevent, diagnose and treat physical and mental health problems with equal regard”[14]. Secondary care is delivered in NHS Trusts. Each Trust has its own Chief Executive and leadership team and while they are governed by central NHS legislation, each Trust works as an independent entity. The configuration and delivery of services is therefore unique to each Trust, ensuring that each geographical region in England has access to essential healthcare services. Healthcare delivery by a Trust could be provided in a single hospital providing all the required services or it could be a merger of multiple hospitals in the geographical area each providing specific services (for example: https://www.uclh.nhs.uk/OurServices/OurHospitals/Pages/Home.aspx)[15].

The model of specialised TYA cancer care implemented from 2005 focused on 13 TYA Principal Treatment Centres (TYA-PTC) in England. These were based in 13 different Trusts, selected to complement the existing services delivered in children’s cancer units (aged up to 16 years in the main but local variation would accept older teenagers) and adult cancer services from 18 years onward. The TYA-PTCs were funded to deliver specialist care, which included the same standard of cancer care as the children and adult units but care was enhanced by the addition of age-appropriate environments and multi-disciplinary teams experienced in working with TYA. For example, providing education and career support to enable TYA to continue with education and employment at a critical time in their lives; nurse specialists who were skilled at discussing challenging subjects (sex, fertility, drug and alcohol use); space to interact with other TYA with cancer to promote normal development and youth support coordinators who provide youth support and facilitate peer to peer activities(see Morgan et al[7] for examples of what is included in a TYA unit).

The location of the TYA-PTCs were chosen based on a number of factors, including existing established service, geographical location and other cancer services available. The guidance directed that TYA aged 16-18 years must be treated in a TYA-PTC, while young adults aged 19-24 years were to be offered the choice to receive care in a TYA-PTC or a local cancer unit that could provide their cancer treatment and some aspects of age-appropriate care. There was variation in the lower age of admission in TYA-PTCs based on history and availability of other services locally so this resulted in TYA aged 13-16 being treated in a children’s cancer unit or TYA-PTC and those aged 17-24 could be admitted to a TYA-PTC or adult cancer unit. By 2010, about two-thirds of those aged 15-18 years and one-third of 19-24-year olds were believed to have contact with a TYA-PTC[16]. Place of care was therefore directed by clinicians based on cancer type and geographical location. While there is an international mobilisation to implement specialist TYA services[12], including in other European countries, Australasia and North America, the impact of such services on clinical outcomes has not been robustly evaluated.

The BRIGHTLIGHT study is a prospective evaluation of the benefits of specialist TYA services in the English NHS. In order to capture the complexity of the delivery of TYA cancer care, it comprised an evaluation from the perspective of the environment of care [17], the workforce delivering care [18] and young people receiving care. BRIGHTLIGHT was developed with extensive input from young people as well as health professionals [6, 9, 19]

and based on consultation with young people[20]. This included input into the selection of the primary outcome: quality of life (QOL).

Quality of Life is defined as "…subjective, multidimensional and dynamic. It is unique to each individual and includes aspects of physical, psychological and social function. It is dependent not only upon the stage of development but also the illness trajectory. This involves the achievement of goals and aspirations and the constraints imposed through ill health and treatment"[21]. Measurement of QOL uses the patient's own report to evaluate the spectrum of impact of illness upon them and has become an increasingly valued healthcare outcome. Previous reports of young people's QOL after a cancer diagnosis have shown this to be significantly lower than normative population data[22]. Longitudinal assessment has indicated QOL improved in the first year after diagnosis but there was no significant improvement in the second year [23]. No evaluation beyond the second year has been reported and while studies have investigated predictors of QOL there has been no evaluation of the impact of different models of delivery of care on QOL. We examined QOL at 6, 12, 18, 24 and 36 months after diagnosis in relation to the proportion of care young people received in a TYA-PTC

METHODS

Study design

The BRIGHTLIGHT study is a mixed methods programme of research. Results from an embedded longitudinal cohort study, obtaining data from young people through a bespoke survey[24], are reported here. The survey was administered at five time points during the first three years after diagnosis (6, 12, 18, 24 and 36 months, waves 1-5 respectively). A scale was developed, previously described in detail[25], using Hospital Episode Statistics (HES) in-patient data to measure episodes of care in different NHS Trusts and then used to assign young people to one of three levels of TYA care dependent on how much in-patient HES activity recorded in the first 12 months after diagnosis was delivered in a TYA-PTC: no care in a TYA-PTC, i.e., all care was delivered in a children's or adult cancer unit (NO-TYA-PTC), some care delivered in a TYA-PTC with additional care in a children's or adult cancer unit (SOME-TYA-PTC) or all care delivered in a TYA-PTC (ALL-TYA-PTC).

Patient and public involvement

BRIGHTLIGHT has been developed with young people from the point of inception and our Young Advisory Panel (YAP) have been involved in the management, implementation and dissemination of the study. This has been reported in detail previously [20, 26-29] but in summary, BRIGHTLIGHT was developed based on consultation with young people attending a patient conference in 2008: place of care was identified as the third priority for future research. Young people worked with the research team to conduct the research informing the National Institute for Health Research grant application[6] including representation as a co-applicant. The YAP have advised on changes to recruitment[28], helped develop the retention strategy[26], informed additional studies[29], and are involved in dissemination[30].

Participants and setting

BRIGHTLIGHT was open to recruitment between October 2012 and April 2015 in 109 English NHS hospitals of which 97 recruited at least one young person. Eligibility was defined as aged 13-24 years at the time of diagnosis, newly diagnosed with cancer (ICD-10 codes C00-C97) and recruited within four months of diagnosis. There was no eligibility exclusion for a language or sensory impairment affecting communication. The following groups were excluded: those serving a custodial sentence; not anticipated to be alive at the first point of data collection (6-months after diagnosis); or incapable of completing a survey. Details of the recruitment process are reported elsewhere[25,31]. Young people gave written consent and parental consent was also obtained for those less than 16 years. Checks were made through the Demographic Batch Service at NHS digital before each wave of data collection to ensure young people were alive and to obtain their most recent address. The study was approved by London-Bloomsbury NHS Research Ethics Committee and the Confidentiality Advisory Group of the Health Research Authority.

The sample size calculation was based on a comparison between the three levels of TYA care[25] for the primary outcome of PedsQL total score[32], measured at five time points over the three-year follow-up. Previously reported PedsQL data for childhood cancer patients suggested a standard deviation for this score of 16[33]. To detect a difference in scores of 8 units with 80% power[34] required a sample of 200 young people. This calculation assumed a significance level of 0.01 (2 sided) to allow for multiple comparisons between three levels of TYA care and assumed an average of three repeated measurements per patient (intra cluster correlation 0.3 as suggested as a maximum for similar patient outcomes[35]). The calculation allowed for adjustment for confounding factors using a variance inflation factor with a correlation of 0.5[36]. To ensure adequate power to examine the effect of TYA care on QOL within subgroups of age at diagnosis (13-18 and 19-24 years) and type of tumour (haematological, solid tumour groups), the minimum required sample size was raised to 800 (80% power).

Data collection

Data were collected from three sources: young people's self-report, patient clinical records, and NHS and Public Health England (PHE) databases. Details of these data sources are reported elsewhere[25]. Data presented here are responses to the BRIGHTLIGHT Survey, a bespoke survey containing five validated questionnaires and 169 descriptive questions related to post diagnosis experience. The survey was administered through face-to-face interviews in young people's homes by an independent research company at the first time point and either online or telephone interview at subsequent waves of data collection[24].

This paper reports data for the primary outcome, QOL, which was measured using the Pediatric Quality of Life Questionnaire (PedsQL)[32]. At the time of study development this was the only measure of QOL validated for teenagers and young adults[37]. It contains 23 items rated using a five-point Likert Scale (Never, Almost never, Sometimes, Often, Almost always). Responses are presented as four domain scores (physical, emotional, social, and work/studies functioning), two summary scores (physical and psychosocial function) and a total score. Domain, summary and total scores range from 0-100, with 100 representing the best possible QOL.

Analysis

Analysis was carried out following a predefined statistical analysis plan using STATA version 15. A mixed effects model was used to investigate the relationship between the levels of TYA care and the PedsQL total score, allowing for repeated measurements taken over the 3 years since diagnosis. The model was adjusted for confounding factors identified based on the conceptual model underpinning the BRIGHTLIGHT Survey[6,24] and using a causal diagram in the form of a Directed Acyclic Graph (DAG) (DAGitty software www.dagitty.net; Supplemental File, Figure A1). Factors adjusted for were age at diagnosis, type of cancer (leukaemia, lymphoma, brain and central nervous system, bone tumours, sarcoma, germ cell, melanoma, carcinomas, other), socioeconomic status (Index of Multiple Deprivation (IMD)[38] quintile), severity of cancer (least, intermediate, most[25]), ethnicity (white, other), choice offered about where to receive treatment (yes/no), presence of any long term condition prior to cancer (yes/no), days from first symptom to diagnosis and number of General Practitioner visits before diagnosis. Geographical location (specified as 12 cities, derived from the TYA-PTC and their network of hospitals) was included in the model as a random effect. Models were extended to include interaction terms to investigate predefined subgroup effects by age at diagnosis (both as a continuous factor and using categories of 13-18 and 19-24 years) and tumour type (haematological and solid tumours). An interaction with time since diagnosis was also examined to investigate whether the relationship between level of TYA care and QOL changed over time. Similar models were fitted for the PedsQL domain scores for physical, social, emotional and work/school/college functioning, and the psychosocial summary score.

The extent and patterns of missing QOL data over time were examined using summary statistics and profile plots. As there is no provision in the scoring of PedsQL to directly account for death, our main analysis did not distinguish between data 'missing' following death and that missing for other reasons. With the possibility of informative missing data due to deaths, a sensitivity analysis was carried where joint mixed-effect models for the longitudinal QOL scores and time until death were fitted to account for the correlation between the QOL and survival outcomes[39]. The QOL estimates for the effect of level of TYA care were then compared with those obtained from previously fitted mixed models.

RESULTS

A total of 1,126 young people were recruited. BRIGHTLIGHT survey data at wave 1 were available for 830 (75%) participants and details of numbers at each wave are summarised in Figure 1. Characteristics of those who did and did not complete wave 1 were similar, except for a higher proportion of non-white participants not completing wave 1 (12% vs. 19%, p=.004) [25]. Forty-eight participants could not be assigned a level of TYA-PTC care as there were no linked HES inpatient records available. Data from 782 young people were therefore included. There were fewer young people receiving ALL-TYA-PTC care (n=193; 25%) in comparison to SOME-TYA-PTC (n=312; 40%) and NO-TYA-PTC (n=277; 35%). Demographic characteristics and summary of variables adjusted for in the analysis are shown in Table 1. Young people who received NO-TYA-PTC care were slightly older, more likely to be working full/part time, had less severe disease, had a better prognosis and were more likely to have been given a choice in their place of care. Young people who had ALL-TYA-PTC care were more likely to come from less deprived areas.

Table 1: Participant characteristics according to level of care at wave 1

Characteristic		Level of TYA care at 12 months from diagnosis		
		NO-TYA-PTC N=277	**SOME-TYA-PTC N=312**	**ALL-TYA-PTC N=193**
Age at diagnosis (years)	Mean (SD)	21·04 (3.01)	19·40 (3.41)	19·97 (3.15)
Age groups	13-15 years 16-18 years 19-24 years	37 (10%) 34 (10%) 288 (80%)	72 (17%) 128 (31%) 215 (52%)	40 (15%) 78 (29%) 152 (56%)
Gender	Male Female	148 (53%) 129 (47%)	165 (53%) 147 (47%)	112 (58%) 81 (42%)
Ethnicity*	White Mixed Asian Black Other	252 (91%) 4 (1%) 15 (5%) 4 (1%) 2 (1%)	273 (88%) 5 (2%) 24 (8%) 7 (2%) 3 (1%)	163 (84%) 4 (2%) 20 (10%) 2 (1%) 4 (2%)
Socioeconomic status (IMD quintile)	1 – most deprived 2 3 4 5 – least deprived	66 (24%) 47 (17%) 51 (19%) 65 (24%) 46 (17%)	73 (24%) 52 (17%) 60 (20%) 61 (20%) 59 (19%)	34 (18%) 32 (17%) 37 (20%) 40 (21%) 46 (24%)
Marital Status	Married/civil partnership Cohabiting Single/divorced	9 (4%) 43 (17%) 198 (79%)	8 (3%) 27 (10%) 227 (87%)	6 (3%) 18 (10%) 148 (86%)
Current status	Working full/part time In education Other work (apprentice/intern/voluntary)	126 (45%) 61 (22%) 6 (2%)	72 (23%) 112 (36%) 5 (2%)	43 (22%) 81 (42%) 6 (3%)

	Unemployed	10 (4%)	11 (4%)	7 (4%)
	Long term sick	39 (14%)	51 (16%)	31 (16%)
	Not seeking work	35 (13%)	61 (20%)	25 (13%)
Type of cancer (Birch classification)				
	Leukaemia	19 (7%)	49 (16%)	33 (17%)
	Lymphoma	111 (40%)	75 (24%)	70 (36%)
	CNS	9 (3%)	9 (3%)	12 (6%)
	Bone	7 (3%)	59 (19%)	3 (2%)
	Sarcomas	8 (3%)	31 (10%)	15 (8%)
	Germ cell	64 (19%)	55 (18%)	31 (16%)
	Skin	22 (8%)	1 (<1%)	4 (2%)
	Carcinomas (not skin)	41 (15%)	31 (10%)	23 (12%)
	Miscellaneous specified**	5 (2%)	2 (<1%)	1 (<1%)
	Unspecified Malignant	1 (<1%)	0	1 (<1%)
Severity at diagnosis (row %, column %)				
	Least	200 (46%, 72%)	133 (31%, 43%)	95 (22%, 49%)
	Intermediate	49 (26%, 18%)	82 (44%, 26%)	56 (30%, 29%)
	Most	28 (17%, 10%)	97 (58%, 31%)	42 (25%, 22%)
Prognostic score				
	<50%	21 (8%)	60 (19%)	41 (21%)
	50-80%	54 (20%)	125 (40%)	44 (23%)
	>80%	200 (73%)	126 (41%)	108 (56%)
Location* **				
	Birmingham	41 (15%)	59 (19%)	12 (6%)
	Bristol	51 (18%)	32 (10%)	4 (2%)
	Cambridge	12 (4%)	8 (3%)	1 (1%)
	Manchester	22 (8%)	35 (11%)	11 (6%)
	Merseyside	13 (5%)	11 (4%)	6 (3%)
	East Midlands	15 (5%)	24 (8%)	60 (31%)
	Leeds	20 (7%)	25 (8%)	25 (13%)
	Newcastle	13 (5%)	6 (2%)	24 (12%)
	Oxford	5 (2%)	4 (1%)	7 (4%)

	London Sheffield Southampton	60 (22%) 7 (3%) 18 (7%)	83 (27%) 9 (3%) 16 (5%)	10 (5%) 9 (5%) 24 (12%)
Given a choice about where to receive treatment[$]	 Yes No (or < 19 years)	N=272 121 (45%) 151 (56%)	N=311 86 (28%) 225 (72%)	N=192 48 (25%) 144 (75%)
Long term condition prior to cancer	 Yes No	N=277 20 (7%) 257 (93%)	N=311 34 (11%) 277 (89%)	N=193 18 (9%) 175 (91%)
Time to diagnosis: days from 1st symptom	Median (IQR), [min, max]	N=264 62 (29·5 to 168·5) [0, 1340]	N=304 65·5 (29·5 to 152·5) [0, 959]	N=188 63·5 (25·5 to 151·0) [0, 1217]
Time to diagnosis: number of GP visits before diagnosis	Median (IQR), [min, max]	N=274 1 (0 to 3) [0, 20]	N=311 1 (0 to 3) [0, 20]	N=193 2 (1 to 3) [0, 40]

* Wave 1 data was used with missing values completed using available PHE data.

** includes 4 'unclassified' – treated in cancer unit but did not have cancer

***Includes the TYA-PTC and hospitals linked to the multi-disciplinary team at the TYA-PTC; where available based on hospital of diagnosis, for 77 cases based on recruiting hospital

$ Those <19 years at diagnosis were assumed not to have been given a choice

Longitudinal changes in the average QOL total score according to the level of care are shown in Figure 2 (summary by wave is given in Supplemental file, Table A1). Across all time periods this illustrates lower QOL score for those in the SOME and ALL-TYA-PTC groups compared to the NO-TYA-PTC group. Differences between level of care appeared to diminish steadily over time. The negative coefficients for levels of care from the model indicate that across the 3 year period of the study QOL scores were on average higher for those with NO-TYA-PTC care compared with SOME-TYA-PTC and ALL-TYA-PTC with a larger difference compared with the SOME-TYA-PTC category (Table 2). The differences were statistically significant but fell inside the threshold of 8 points proposed to be clinically significant [32]. There was no evidence that the relationship between QOL and level of care was different for the combined group of leukaemia/lymphomas compared with other cancers. Also, there was no evidence of a difference by age at diagnosis (Figure 3). There was evidence that the QOL/Level of care relationship changed over time such that differences between the groups diminished i.e. slopes for SOME-TYA-PTC and ALL-TYA-PTC over time are steeper than for NO-TYA-PTC, therefore rates of improvement of QOL were superior in the ALL-TYA-PTC and SOME-TYA-PTC (Table 3), mirroring what was seen in Figure 2.

Analysis of the physical functioning and work/school/college functioning domain scores showed a similar pattern to that seen for the total QOL score. The SOME-TYA-PTC group had a mean difference in physical functioning of -8.28 compared to the NO_TYA-PTC group, which was statistically significant and above the threshold for clinical significance. For the emotional functioning domain however, difference between groups were less marked and notably the average difference in scores between the SOME-TYA-PTC and NO-TYA-PTC was reduced. Difference between groups in terms of social functioning and the psychosocial summary scores were small and not statistically significant (Figures 4-8, Table 2).

Table 2: Mixed model investigating the relationship between levels of TYA care received during the first 12 months from diagnosis and total quality of life and domain scores over 3 years (N=733)

		Difference in means	95% Confidence Interval	P-value
TOTAL QUALITY OF LIFE SCORE (n=733)				
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-5.63	-8.49 to -2.77	P=0.0005
	ALL-TYA-PTC	-4.17	-7.28 to -1.07	
PHYSICAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-8.28	-11.95 to -4.61	P=0.0001
	ALL-TYA-PTC	-4.79	-8.76 to -0.81	
EMOTIONAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-4.29	-7.79 to -0.80	P=0.015
	ALL-TYA-PTC	-5.43	-9.29 to -1.57	
SOCIAL FUNCTIONING (N=733)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-2.96	-5.77 to -0.16	P=0·099
	ALL-TYA-PTC	-2.49	-5.60 to 0.62	
WORK/SCHOOL/COLLEGE FUNCTIONING (N=595)				
TYA care category (v NO-TYA-PTC)	**SOME-TYA-PTC**	-6.87	-10.45 to -3.30	P=0.0007
	ALL-TYA-PTC	-4.67	-8.47 to -0.87	
PSYCHOSOCIAL SUMMARY SCORE (N=600)				
TYA care category	**SOME-TYA-PTC**	-2.51	-5.71 to 0.70	P=0.074

(v NO-TYA-PTC)	**ALL-TYA-PTC**	-3.96	-7.44 to -0.48	

* results from a three level model for repeated measurements of QOL over time since diagnosis, with a random effect for geography and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis. Missing data for 96 due to missing TYA category and missing data in other covariates
** Likelihood ratio test

Table 3: Investigation of changes in QOL score over time: Results from adjusted* mixed effects models with interaction term (time months x TYA-PTC category). Coefficients for time describe the linear increase in QOL score per month within each TYA care category (N=733)

TYA care category	Coefficient for time (per month)	95% confidence interval	P-value from interaction
NO-TYA-PTC	0·26	0·18 to 0·34	0·004
SOME-TYA-PTC	0·45	0·37 to 0·53	
ALL-TYA-PTC	0·37	0·27 to 0·46	

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Results from post hoc analysis excluding patients with bone tumours were similar to those for all cancers combined (Supplemental file, Table A2). A subgroup investigation of patients with lymphoma, the biggest diagnostic category, showed these were not significantly different from those for the group of other cancer types (Supplemental file, Table A3). Finally, sensitivity analyses using joint modelling for survival alongside longitudinal QOL did not alter the conclusion based on the main results (Supplemental file, Table A4).

DISCUSSION

Our study is the first reported national longitudinal evaluation of specialist cancer services, more specifically TYA-PTCs and their networks of care, as they were originally defined in 2005[3]. We recorded patient outcomes to determine the influence of place of care, and after consultation with patients and professionals, selected QOL as the primary parameter of interest. Using routinely collected hospital admission data to identify time spent in the TYA-PTC, we categorised patients by the level of their care received in the TYA-PTC (all, none or some). We found that there was a statistically significant difference between these groups with those in the NO-TYA-PTC group having superior QOL compared to those in the ALL-TYA-PTC group, whilst those in the SOME-TYA-PTC group reported lowest QOL. Quality of life improved over time in all three groups, but rates of improvement were significantly better for SOME and ALL-TYA-PTC.

We predicted that sociodemographic or disease factors might explain some of the differences between groups and adjusted the analyses for these confounding variables. Despite extensive analysis we were unable to identify other factors to account for these differences. Like other reports of young people's QOL after a cancer diagnosis[22], we found this to be low, irrespective of where young people were treated. We found that young people who did not access a TYA-PTC had better QOL in comparison to those who had all or some of their care in a TYA-PTC. However, while this was statistically significant, the mean

difference between the NO-TYA-PTC and ALL-TYA-PTC groups was not at a level proposed as clinically significant (8-point difference[33]). Nevertheless, it is important to consider reasons for lower QOL when young people experience multiple types of place of care and the determinants of place of care. Based on work in other settings where care is delivered on multiple sites [40] we surmise that this may result from limited coordination of care, perhaps including inadequate communication with and between professionals. Having to repeat conversations and explanations of their cancer diagnosis and treatment details is frequently reported as burdensome to young people[6]. A greater understanding of the determinants of place of care for young people and the factors which influence a sense of care co-ordination deserve further exploration.

It is interesting that young people who had no access to the TYA-PTC rated their QOL the highest. This could reflect young people rating themselves by comparison with the other people they could see being treated for cancer outside of a TYA-PTC, including older adults. It could also be that young people chose to receive care locally rather than travel to the TYA-PTC so they could keep their links to their 'normal' life, which is supported by the domain level analysis where they also rated their work/school/college functioning higher. Alternatively, the strong emphasis placed on the unique issues faced by TYA with cancer by members of the TYA MDT staff may have heightened patients' awareness of these problems in comparison to the NO-TYA-PTC group, and consequently they lowered their perception of their QOL while the NO-TYA-PTC group remained comparatively unaware of such concerns. Future work could focus on the influence of being given a choice in the place where young people receive care, and the factors that young people consider to be important when making this decision.

The longest follow-up for longitudinal assessment of QOL previously reported to two years after diagnosis[23], which showed no improvement after the first year. However, we found that there was a gradual improvement in QOL over 3-years, which was more rapid when young people received all their care in a TYA-PTC. The philosophy of TYA cancer care includes the delivery of care to support young people to achieve their long-term personal outcomes (education, employment and relationships), the benefits of care provided by the TYA-PTC may therefore not be realised in the short-term. It would be beneficial for us to understand whether this improvement continued into long-term survivorship, especially the influence of QOL reaching and sustaining goals such as employment.

There are several limitations to this study including how specialist care was defined and measured. This was based on the location of the 13 NHS Trusts in England commissioned as TYA-PTCs but not the specific hospitals within these Trusts where the specialist TYA services were based. For example, a Trust which included multiple hospitals could only have specialist TYA services in one therefore a young person receiving care in one of the other hospitals was assumed to have had access to specialist TYA services, i.e., they were assigned to the ALL-TYA-PTC group rather than NO-TYA-PTC. Furthermore, using the Trust commissioned as a TYA-PTC does not capture the details of the TYA-specific care available or delivered and assumes that this is equal in all. We know there was wide variation in the delivery of care through the duration of the study[41]. However, at the time of study inception HES was the sole data source available that would allow an objective measurement of place of care. In complementary work, the key elements of specialist age-appropriate care for TYA

have been described[17]. This would provide an alternative categorisation against which to measure patient and clinical outcomes.

The cohort represented approximately a fifth of the total cancer population diagnosed between July 2012 and December 2014 as ascertained through the National Cancer Registration and Analysis Service, and there were differences in cancer types between the cohort and those not recruited[25], which could impact on the generalisability of the results. For example, the cohort included a higher proportion of young people with germ cell tumours and lymphoma, but a lower proportion of carcinoma and skin cancers. We used a single mode of survey administration at wave 1, and multiple modes at waves 2-5. While this may have introduced a social desirability bias (noted to be more so for telephone interviews than web-based surveys[42]), this was to increase the response rate as work during the feasibility study for BRIGHTLIGHT indicated no one method was acceptable to all young people. Finally, we used a measure of QOL that was validated across the age 13-24 years[37], but this may not reflect the issues that were most relevant to young people with cancer in the UK (having been developed in the US in a non-cancer population). This is supported by comments made in the cognitive interviews undertaken when the survey was being developed; young people did not agree with the wording of the school functioning domain, so this was changed to work/school/college[24]. However, young people who were not in education, employment or training would not be able to answer these questions. Future work is required to develop TYA-specific QOL measures that reflect issues specific to this population.

Despite these limitations this is the first systematic prospective evaluation of specialist services for young people with cancer. We have found that TYA cancer care as commissioned in 2010 resulted in young people's QOL gradually improving 3-years after diagnosis and improving more rapidly from a lower baseline if young people's treatment involved a TYA-PTC. NHS care pathways may result in care in specialist centres for young people with the poorest initial QOL, and local care for those with the least poor initial QOL, risk stratifying the patients appropriately. Young people who receive some care in both a children's or adult cancer unit and at a TYA-PTC also have an improvement in QOL, but the rate of improvement was less and QOL remained lower than for young people treated in a single type of organisation. The factors influencing place of care and the differences in QOL and survival remain unclear. A model of 'joint care', increasing the emphasis and investment in communication between TYA-PTCs and other Trusts designated to deliver elements of TYA cancer care, is currently proposed by the NHS in England. The influence of such changes in care provision should be examined prospectively in future to identify if QOL of young people with cancer is improved wherever care is received.

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Author contributions:
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, SL, AM, RF, DS, JSW contributed to the analysis. 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 are 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 2020 when the primary analysis is complete. We welcome collaboration, for general data sharing enquiries please contact RMT (rtaylor13@nhs.net).

Figure legends

Figure 1: Participation at each wave of data collection

*Drop-outs between waves due to death, permanent optout 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 2: Mean PedsQL total score over time since diagnosis (with 95% confidence intervals)

Graph based on data collected in Waves 1 to 5, plotted against median time since diagnosis.

Figure 3: Subgroup investigations for cancer type (leukaemia/lymphoma v other) and age group (<19 v 19+): Results from adjusted* random effects models with interaction terms (N=733)

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, Choice about where to receive treatment, Long term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Figure 4: Mean PedsQL physical functioning domain scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 5: Mean PedsQL emotional functioning domain scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 6: Mean PedsQL social functioning domain scores over time since diagnosis (with 95% confidence intervals)

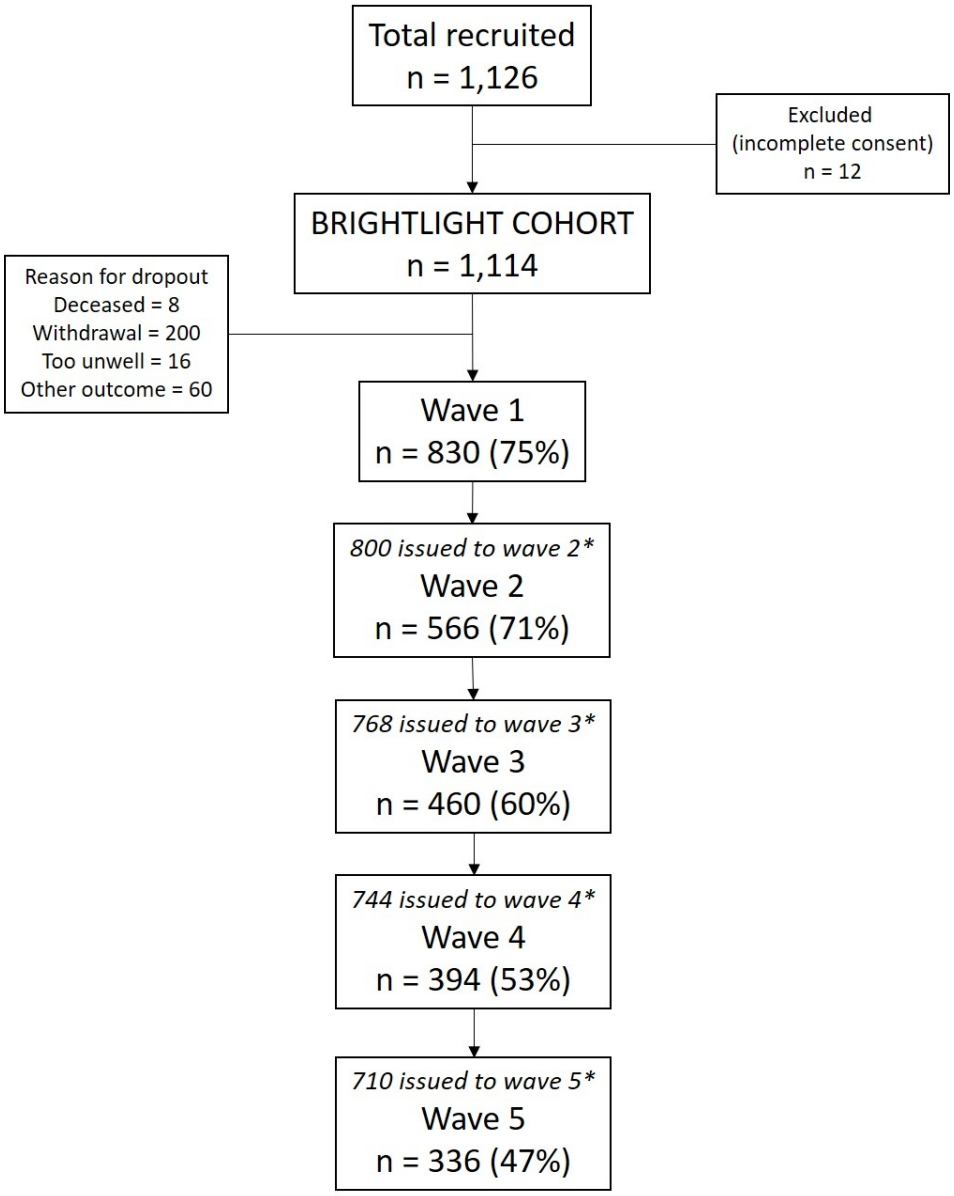
(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 7: Mean PedsQL work/school/college functioning domain scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)

Figure 8: Mean PedsQL Psychosocial summary score scores over time since diagnosis (with 95% confidence intervals)

(Graphs based on data collected in Waves 1 to 5, plotted against median time since diagnosis.)



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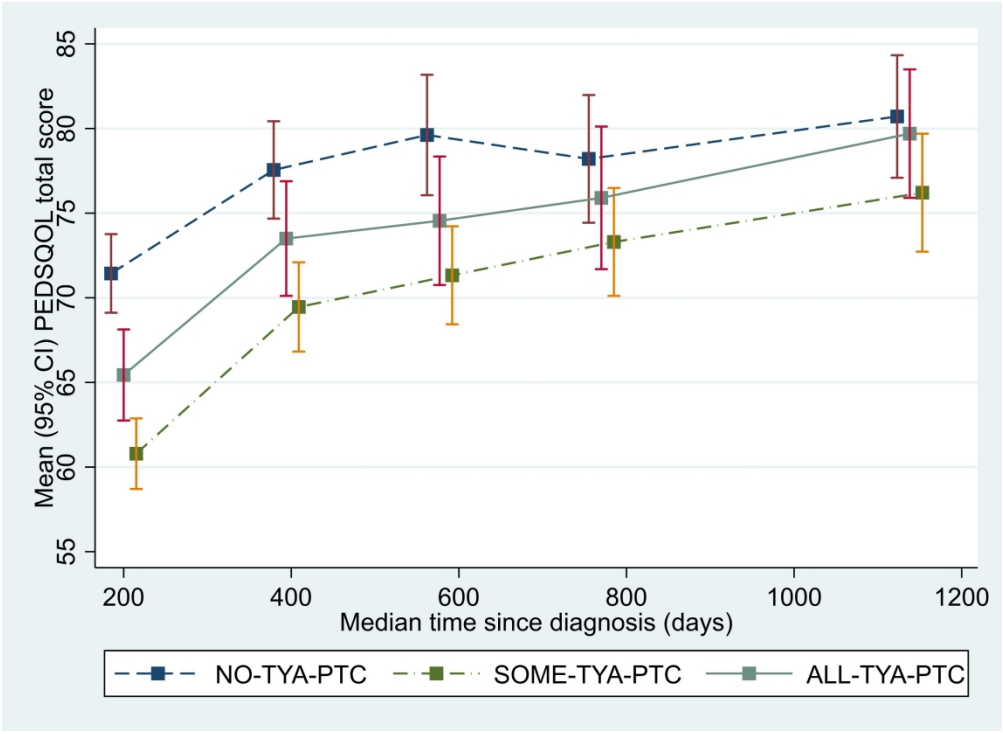

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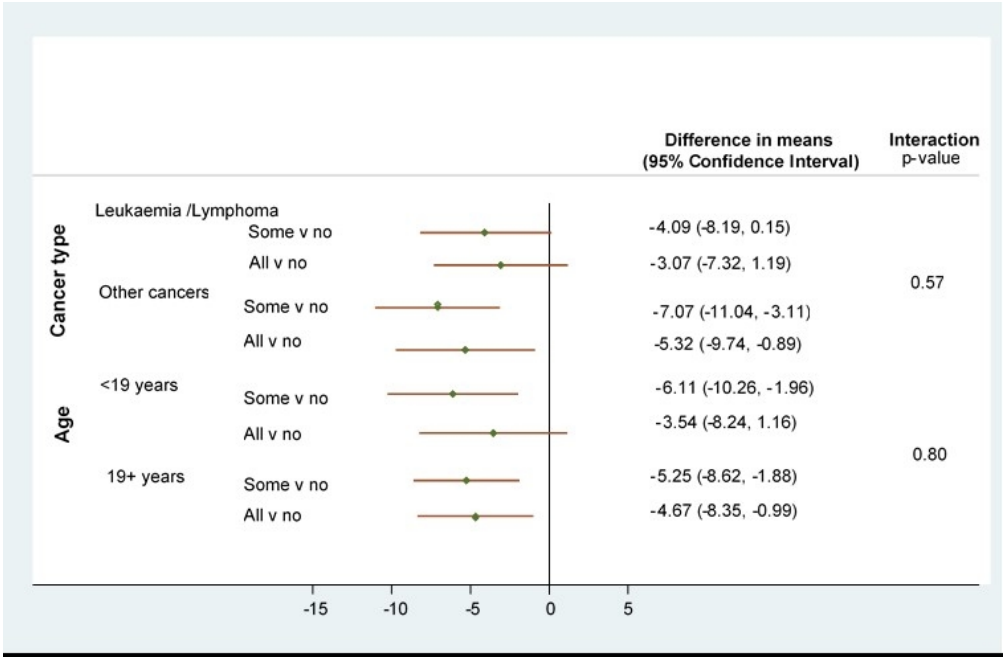

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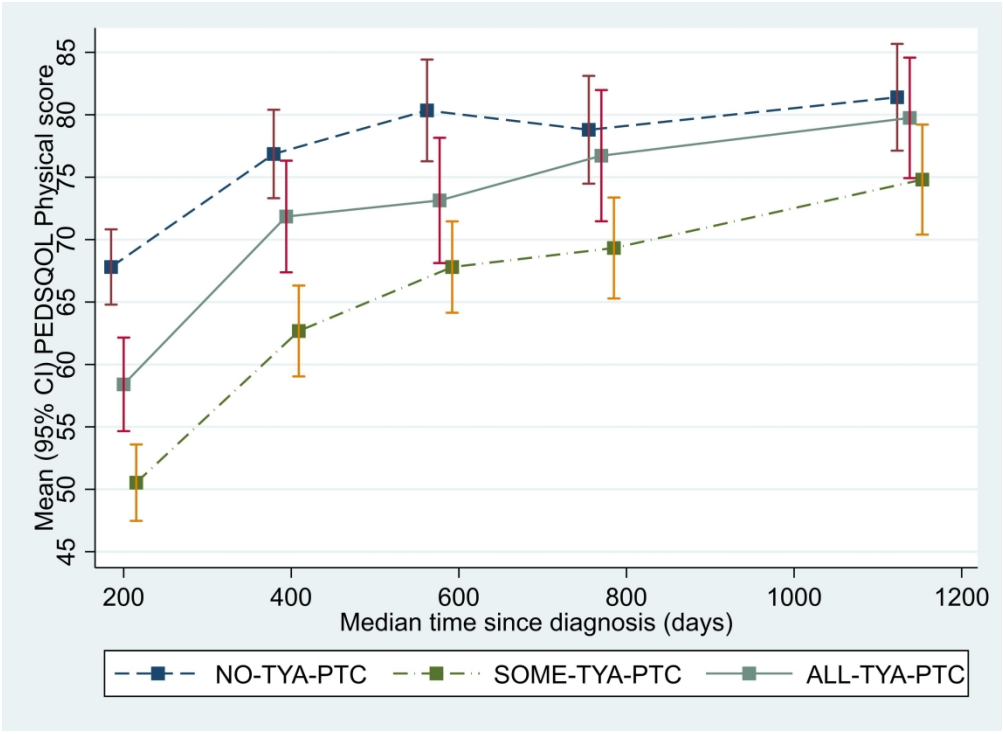

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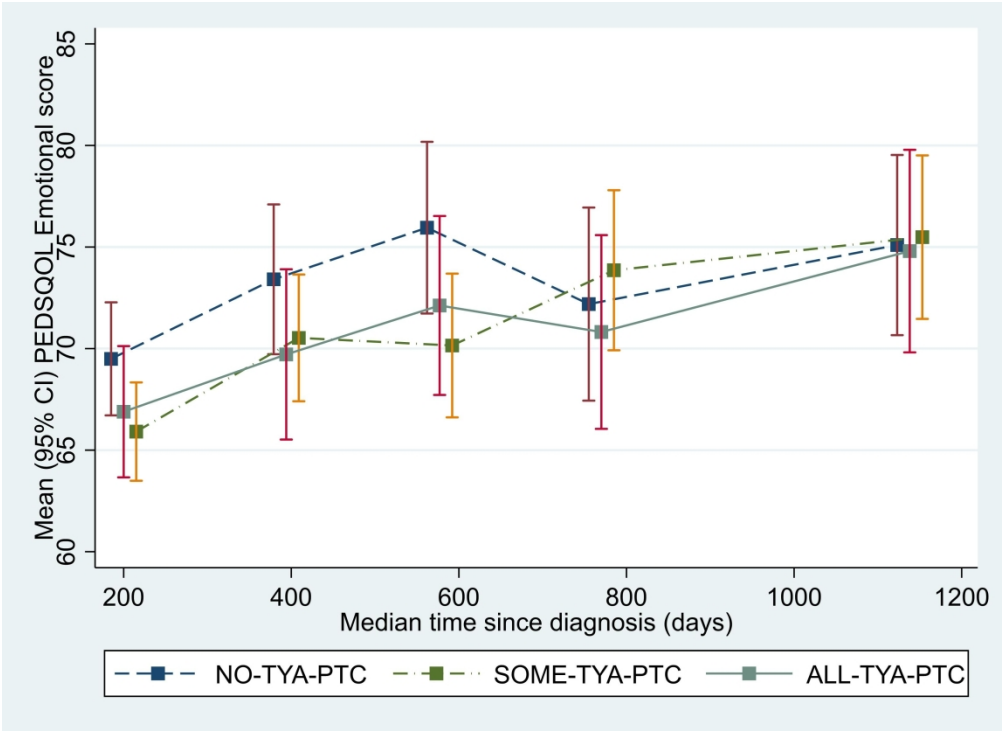

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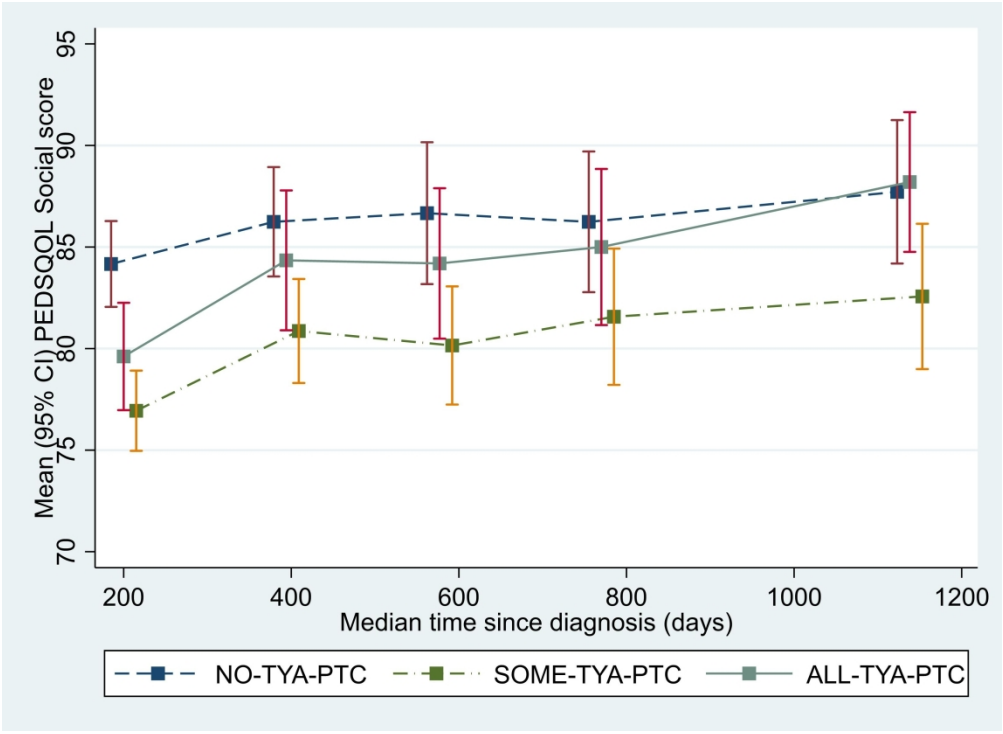

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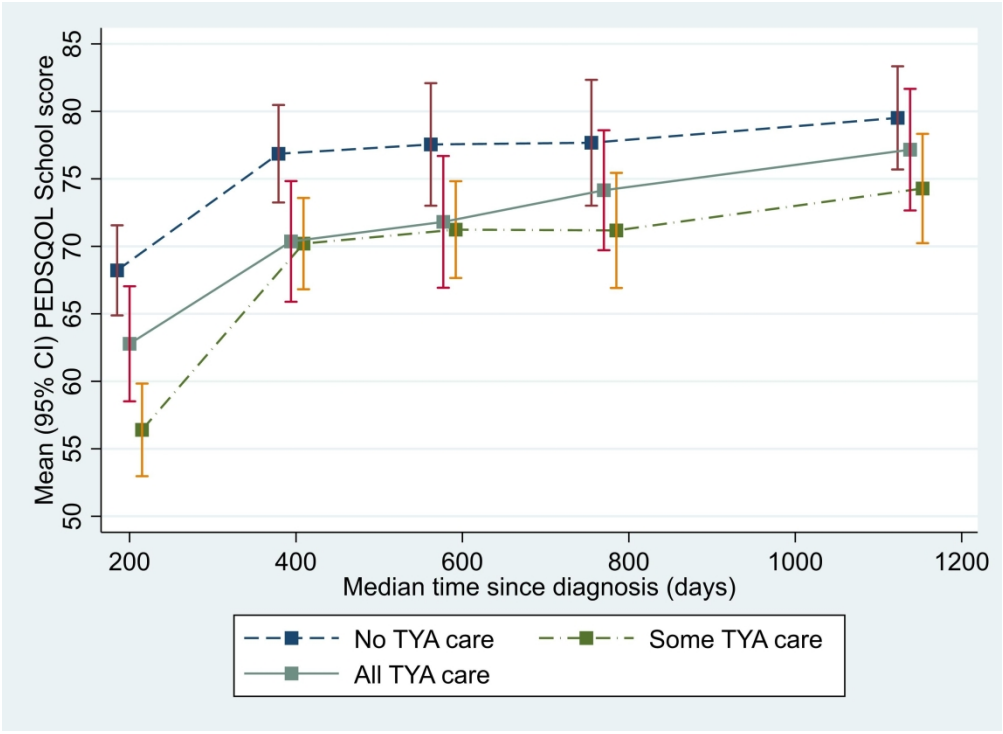

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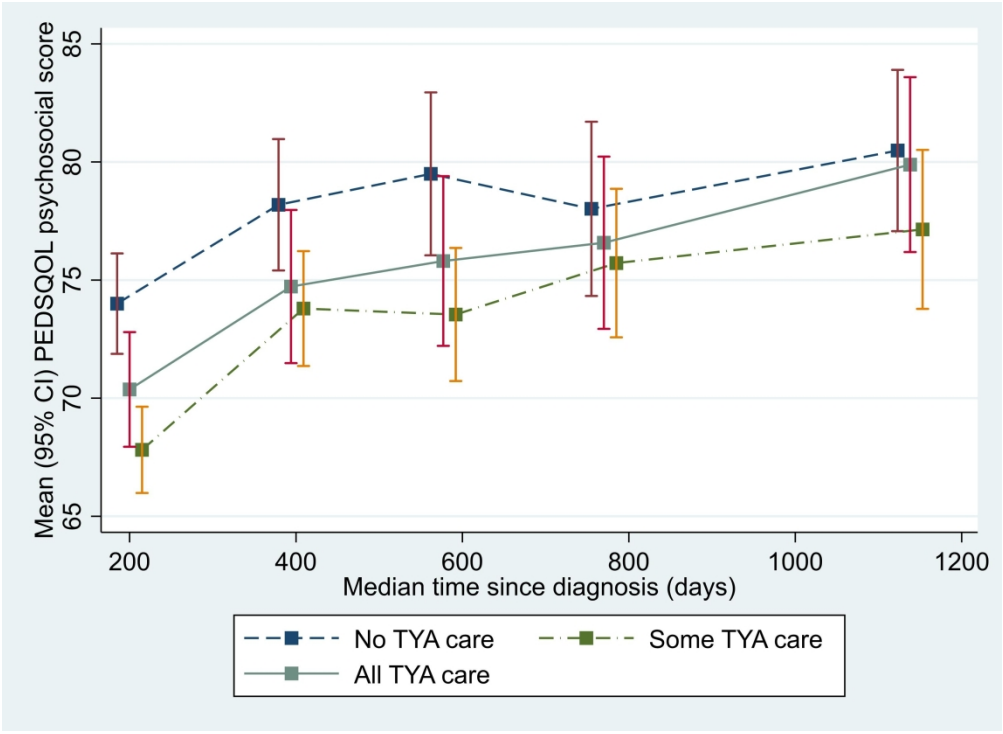

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Supplemental file

Figure A1: Matrix representing the causal diagram explaining confounding variable to enter in the Directed Acyclic Graph (DAG)

	TYA SCL	QOL	Age	Choice	CS	CT	DoH	Ethnicity	Finances	Gender	Geography	I&C	LTC	RtD	SE	SES	SS	Treat-ment
TYA SCL		↗	↗	↗	↗	↗	↗	↗	↗	O	↗	↗	↗	↗	↗	↗	↗	↗
QOL			↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗
Age				↗	O	↗	↗	O	↗	O	O	↗	↗	↗	↗	↗	↗	↗
Choice					↗	↗	O	↗	↗	O	↗	↗	↗	↗	↗	↗	↗	↗
CS						↗	↗	↗	↗	O	↗	↗	↗	↗	↗	↗	↗	↗
CT							↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗
DoH								↗	↗	↗	↗	↗	↗	↗	↗	↗	↗	↗
Ethnicity									↗	O	↗	↗	↗	↗	↗	↗	↗	↗
Finances										O	↗	↗	↗	↗	O	↗	↗	↗
Gender											O	↗	↗	↗	↗	O	↗	↗
Geography												↗	↗	↗	↗	↗	↗	↗
I&C													↗	↗	↗	↗	↗	↗
LTC														↗	↗	↗	↗	↗
RtD															↗	↗	↗	↗
SE																↗	↗	↗
SES																	↗	↗
SS																		↗
Treatment																		

CS: cancer severity; CT: cancer type; DoH: duration of hospitalisation; I&C: information & communication; LTC: long-term condition; QOL: quality of life; RtD: route to diagnosis; SE: symptom experience; SES: socioeconomic status; SS: social support

O – indicates a null relationship

Table A1: PedsQL total score by Wave of data collection

	NO-TYA-PTC			SOME-TYA-PTC			ALL-TYA-PTC		
	N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)	N	Mean (SD)	Median (IQR)
Wave 1	276	71.44 (19.68)	73.22 (57.61 to 89.13)	312	60.79 (18.79)	59.71 (47.52 to 75.00)	193	65.44 (19.07)	66.30 (52.78 to 80.56)
Wave 2	173	77.55 (19.31)	83.70 (61.96 to 93.48)	209	69.46 (19.45)	71.74 (54.35 to 85.87)	122	73.50 (19.08)	77.17 (58.33 to 88.04)
Wave 3	126	79.62 (20.38)	85.87 (68.48 to 95.65)	164	71.33 (18.91)	73.76 (59.75 to 84.78)	99	74.55 (19.26)	80.43 (59.72 to 91.30)
Wave 4	121	78.21 (21.16)	84.78 (64.13 to 95.65)	118	73.30 (33.33)	76.24 (60.87 to 86.96)	98	75.90 (21.27)	82.61 (61.96 to 93.48)
Wave 5	103	80.71 (18.75)	86.96 (71.74 to 95.65)	113	76.21 (18.90)	78.26 (65.22 to 93.48)	75	79.70 (16.78)	85.87 (70.65 to 91.30)

Table A2: Results from adjusted mixed effects models investigating the relationship between levels of TYA care received during the first 12 months from diagnosis and the quality of life – excluding bone cancer (N=667)

		Difference in means	95% Confidence Interval	P-value
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-6.02	-9.02 to -3.02	P=0.0003
	ALL-TYA-PTC	-4.53	-7.72 to -1.35	

* results from a three level model for repeated measurements of QOL over time since diagnosis, with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Table A3: Subgroup investigation for lymphoma v other cancer: Results from adjusted* mixed effects models with interaction terms (N=733)

	TYA care category	Adjusted difference in means	95% confidence interval	P-value from interaction
Cancer type				
Lymphoma	SOME-TYA-PTC v NO-TYA-PTC	-6.01	-9.58 to -2.44	0.90
	ALL-TYA-PTC v NO-TYA-PTC	-4.13	-8.08 to -0.17	
All other cancers	SOME-TYA-PTC v NO-TYA-PTC	-4.89	-9.63 to -0.16	
	ALL-TYA-PTC v NO-TYA-PTC	-4.31	-9.18 to 0.55	

* model with a random effect for city and adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis.

Table A4: Results from a joint model of longitudinal quality of life scores and survival investigating their relationship with level of TYA care received during the first 12 months from diagnosis (N=733)*

		Difference in means	95% Confidence Interval
TYA care category (v NO-TYA-PTC)	SOME-TYA-PTC	-6.45	-9.34 to -3.56
	ALL-TYA-PTC	-6.11	-9.58 to -2.64

* Models fitted using Stata command *stjm* with a Weibull submodel for survival (reference: M Crowther, K Abrams, P Lambert. Joint modelling of longitudinal and survival data. The Stata Journal (2013) **13**, Number 1, pp. 165–184)Adjustment for time since diagnosis, age at diagnosis, type of cancer, socioeconomic status, severity of cancer, ethnicity, choice about where to receive treatment, long-term condition prior to cancer, days from 1st symptom to diagnosis, number of GP visits before diagnosis and city (as a fixed effect as a three level model could not be fitted).

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

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	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5 (reference cited for details)
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	na
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
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	5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	6
		(*c*) Explain how missing data were addressed	6
		(*d*) If applicable, explain how loss to follow-up was addressed	6
		(*e*) Describe any sensitivity analyses	6

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	6, reference cited, also supplemental file
		(b) Give reasons for non-participation at each stage	supplemental file
		(c) Consider use of a flow diagram	supplemental file
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	8
		(b) Indicate number of participants with missing data for each variable of interest	supplemental file
		(c) Summarise follow-up time (eg, average and total amount)	supplemental file
Outcome data	15*	Report numbers of outcome events or summary measures over time	supplemental file
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	11
		(*b*) Report category boundaries when continuous variables were categorized	na
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	na
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11 and supplemental file
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-14
Generalisability	21	Discuss the generalisability (external validity) of the study results	13-14
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	16

*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.