Describing the variation in hospital activity following diagnosis with cancer for childhood and adolescent cancer in Yorkshire

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The candidate confirms that the work submitted is her own, except where work which has formed part of jointly authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

Publications

Chapters 6 and 8 contain work based on the following publication:

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Abstract

This study aimed to provide a comprehensive assessment of hospital utilisation among children and young people (CYP), addressing recommendations emerging from the *Children and Young People's Health Outcomes Forum* that emphasised the importance of improving the health of young people. The burden of care for CYP with cancer on local and national healthcare systems is unknown and lack of data limits the ability to inform and improve service delivery. Therefore, I used a specialist population-based cancer register in CYP from Yorkshire, linked to hospital admissions data, to analyse healthcare utilisation after diagnosis and treatment for cancer. Additionally, clinical and sociodemographic factors that contributed to hospital utilisations during and after treatment were identified and discussed.

The study included 3,151 cases of cancer aged 0-29 years diagnosed in Yorkshire during 1996-2009, and admitted to hospital during 1997-2011. The study observed a steady increase in admissions over the period. Children had higher median number of admissions (median=25, Interquartile range (IQR): 8-44) than teenagers and young adults (TYA) (median=10, IQR: 3-20), and spent longer in hospital on average with median duration of three and one days per 100 person-days respectively. However, TYA with leukaemia experienced longer stays in hospital on average than children, with a median duration of eight and four days, respectively. Factors that influenced the pattern of admissions varied by cancer type, however relapse status, type of initial treatment and year of diagnosis were significantly related to hospitalisation independently. Cancer survivors had a significantly higher risk of morbidity compared with the general population after treatment completion (standardised hospitalisation rate (SHR) = 2.37, 95% CI:2.26-2.49).

Findings from this work demonstrate the variation in hospital activity by cancer type and age group, as well as the independent predictors of hospitalisation. This aids the continued development of high-quality cancer services to meet the needs of young people with regard to short-term and long-term care.

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List of Abbreviations

A&E	Accident and Emergency
AIC	Akaike's Information Criterion
ALL	Acute Lymphoid Leukaemia
AML	Acute Myeloid Leukaemia
ASR	Age and Sex Standardised Incidence Rate
BIC	Bayesian Information Criterion
BMT	Bone Marrow Transplant
CCG	Clinical commissioning groups
CI	Confidence Interval
CIP	Continuous Inpatient Spells
CNS	Central Nervous System
CYP	Children and Young People
DAAG	Data Access Advisory Group
DRR	Number of Days in Hospital Rate Ratio
EURAMOS	European and American Osteosarcoma Study Group
FCE	Finished Consultant Episodes
GP	General Practitioner
HES	Hospital Episodes Statistics
HL	Hodgkin Lymphoma
HMRN	Haematology Malignancy Research Network
HRG	Healthcare Resource Groups
HRR	Hospitalisation Rate Ratio
HSCIC	Health And Social Care Information Centre
ICCC	International Classifications of Childhood Cancer
ICD	International Classifications of Disease
ICU	Intensive Care Unit
IMD	Index of Multiple Deprivation
INRG	International Neuroblastoma Risk Group
IQR	Interquartile Range
LCI	Lower Confidence Interval
MI	Myocardial Infarction
N	Number
NA	Not Applicable
NCI	National Cancer Initiative

NHL	Non Hodgkin Lymphoma
NHS	National Health Services
NICE IOG	National Institute for Health and Clinical Excellence Improving Outcomes Guidance
ONS	Office for National Statistics
OPCS	Classification of Interventions and Procedures
PbR	Payment by Result
PHE	Public Health England
PTC	Principle Treatment Centre
SCU	Shared care units
SEER	Surveillance Epidemiology and End Results
SES	Socioeconomic Status
SHR	Standardised Hospitalisation Rate
STS	Soft Tissue Sarcoma
TYA	Teenage and Young Adult
UCI	Upper Confidence Interval
UK	United Kingdom
USA	United States of America
WHO	World Health Organisation
YSRCCYP	Yorkshire Specialist Register of Cancer in Children and Young People

Chapter 1 Introduction

1.1 Motivation

In the UK, more than a third of a million people were diagnosed with cancer in 2013, and 450 deaths caused by cancer each day [1]. Cancer is largely considered to be an elderly disease, as the majority of cancers, constituting almost 50% of cases, were diagnosed among people over the age of 70 [1]. Among children and young people (CYP) aged 0-24 it comprises less than 1% of the total annual incidence [1] and 10% among cases aged 15-24 and 29 years [1, 2], however cancer is the leading cause of natural deaths among this group [3, 4].

The five-year disease-free survival rate for childhood (0-14 years of age) cancer has improved in the last three decades, from 30% to more than 80% for all cancers in general, although it varies across different diagnostic groups [5]. Treatment protocols have improved which have increased survival rates generally but also reduced the number of serious side effects and oncologists are better able to deal with relapsed disease alongside with the development of palliative care to manage end of life care [6]. Although the availability of specialist centres, centralised care, multicentre-trials or standardised treatments have not consistently been improved for each cancer type, there have been improvements across the spectrum of cancer types and there have been no declines in survival over time [6]. Other factors may therefore be attributable to some of the improvements for those cancers where such service improvements were not available which could include changes in patient profiles or characteristics over time. However, older children and young adults (15-24) have not shown similar improvements, which could be explained by the absence of centralised and standardised healthcare facilities and treatments, or limited recruitment into clinical trials, both nationally and internationally other could be due to the differences in biological of the disease and treatment tolerance or due to other multifactorial reasons such as physical and emotional challenges [7, 8].

Based on a comprehensive literature review of the current position in comparison with other countries, the Department of Health in England has undergone major changes in its healthcare services policy with the aim of improving healthcare delivery and outcomes for cancer patients [9]. In 2005, the National Institute for Health and Care Excellence (NICE) published guidelines to improve health outcomes among children and young people with cancer [10]. These guidelines provide CYP with specialist care services,

assuring multidisciplinary communication throughout the healthcare journey. These guidelines were improved in 2009 to allocate shared care services to provide care closer to patients' homes. However, there were variations in the population coverage of specialist services around the UK [11]. The Department of Health aims to provide high quality and equal healthcare services, therefore analysis of the patterns of hospital activity could provide insights into the quality of care delivered to patients, by comparing the usage of hospital resources among patients that had similar diagnoses and treatment protocols, but received care from different providers. Whilst there has been an increase in focus on the long-term effects following cancer for children and TYAs as a result of improved survival, the pattern of healthcare activity, focusing on both short- and medium-term treatment-related comorbidities following diagnosis of cancer, and the variation in uses of healthcare services according to cancer types, age group, gender and place of care after diagnosis have not been comprehensively studied in the published literature. The pattern of hospital admissions has barely been tackled in the UK. There is no evidence on the variation of hospitalisation use by cancer type, or the potential reasons for increases in the rate of hospitalisation among cancer survivors. Furthermore, the rate of hospital encounters after date of diagnosis could highlight short- and long-term treatment-related morbidity that increases the NHS burden and also impacts on patient well-being and quality of life. Understanding the types of hospital admission among cancer survivors could have a potential impact in the ability of healthcare planning to cope with cancer-related comorbidities in the first five years after diagnosis and beyond [12]. A study conducted in France found that the majority of hospital stays for all individuals admitted in 2007 were due to infectious diseases, nervous system complications and cancer treatments (chemotherapy and radiotherapy) [13]. Therefore, cancer and its associated complications had an enormous effect on both the patients and hospital budgets [13]. The French study was not specifically directed at cancer patients, but used a snapshot of cancer survivors from an insurance-based healthcare dataset looking at a range of diseases to provide a broad overview of the usage of hospital resources. The National Institute for Health and Clinical Excellence [2005] suggested that patients, especially TYAs, might be admitted during and after cancer treatment due to alopecia, weight loss or gain, acne, mouth sores, bleeding, infection, amputations, nausea and vomiting, and they are also thought to suffer from coping with these diseases more so than younger children and older adults [11]. This thesis focuses on CYP with cancer by comparing the pattern of hospital activity among CYP cancer survivors by varied demographic and clinical characteristics, such as treatment management factors including: place of care and type of treatment received.

1.2 Study rationale

The NHS Cancer Plan aimed to provide equal services to the population in England [14]. In 2008, the National Cancer Survivorship Initiative was launched in response to the reformation of cancer strategy in 2007. The main objective was to ensure that appropriate services were attained by CYP (aged 0-24) after receiving cancer care. They aimed to motivate survivors to visit follow-up clinics to monitor their health status in both the short and long term. This national initiative was triggered by the fact that there were 40,000 childhood cancer survivors, 60% of which had at least one hospital visit as a result of long-term treatment-related morbidity [15]. The survival rate among TYAs also improved, reaching 83% in 2009 [16]. The increased level of survivors has increased the burden on patient healthcare to cope with cancer and its treatment related comorbidities. CYP survivors spent more time in a hospital compared with their peers, which has huge impact on their overall quality of life and well-being, as well as exhausting hospital resources [17].

Analysis of hospital admissions could provide a solid knowledge base of managing cancer related services, such as treating complications due to cancer or cancer treatments [12, 18, 19]. Seventeen percent of the total acute care unit admissions was for cancer patients of all ages; almost 9% of these could be avoided by referring patients to palliative care [19]. Understanding the pattern of hospital activity among cancer patients could help in predicting cancer consequences, thus enhancing future treatment strategies [20].

Routine assessment is a key element in ensuring that equal services are provided for all patients. Therefore, studying the variation in admission rates adjusting for cancer types and treatment strategies could provide an insight into the amount of care delivered by various healthcare providers. Evidence based literature suggests specialist healthcare providers, such as principle treatment centres (PTCs), provided better outcomes in term of survival rates compared with non-specialist centres [11], more detail on explaining these services is provided in Section 2.4. However, the impact of the type of services provided on outcomes were absent in the literature, i.e. there was no evidence regarding the extent of variations in treatment management and the impact on health outcomes of CYP with cancer. In previous studies it was explained that the poor outcomes among TYAs were driven by the fact that there was inequality in accessing healthcare facilities [21]. As a consequence, studying hospital activity could provide evidence to ensure that patients are treated effectively and efficiently, thereby providing the best outcomes for patients and ultimately leading to fewer complications and, thus, minimising the burden on patients and the NHS. Improvements in healthcare treatments have led to increased rates of survival [22]. However, it raises the concerns of treatment-related complications such as recurrent cancer [23, 24], physical and psychological defects [25, 26] and/or risk

of death among advanced cases or patients with poor prognosis [27, 28]. Childhood acute lymphoblastic leukaemia (ALL) treatment protocols experienced tremendous changes. In the UKALL XI trial, patients were treated at home, which lead to an increase in the mortality rate among patients from lower social classes, since it was difficult to cope with the complexity of these new treatment protocols [29] (more detail in Section 2.3). The results of this research could provide comprehensive knowledge regarding the extent of hospital resources utilised by cancer survivors, to help in planning for services and minimising the allocation of unnecessary resources [18].

1.3 Summary of aims and study questions

The thesis aims to identify the pattern of hospital activity among CYP (aged 0-29 years), taking into account discrepancies in gender, type of initial treatment and place where care was delivered. It will provide an assessment of the quality and equity of using hospital resources among varied healthcare providers (specialists and non-specialists). Consequently, it will provide healthcare commissioners and providers with the health service needs for CYP diagnosed with cancer, in terms of hospital admissions, their length of stay in hospital and related comorbidities from the date of diagnosis both during and following their treatment period. The main study aims and research questions are identified as follows:

1.3.1 Aims

1. To determine whether there has been any change in hospital activity rates post-diagnosis from 1997 to 2011.
2. To assess the variation in hospital activity in terms of the number of admissions and length of stay stratified by admission period (during treatment and after treatment completion) adjusting for treatment length among individuals diagnosed with cancer aged 0-29 years in Yorkshire.
3. To identify the factors that influence the risk of hospital admission and length of stay among leukaemia, lymphomas, central nervous system (CNS) cancers, neuroblastoma, renal tumours, bone tumours, soft tissue sarcomas (STS) and germ cell tumours, adjusting for length of follow-up.
4. To use hospital inpatient admissions to determine the extent of morbidity that lead to hospitalisation in terms of both short-term (during the treatment period) and long-term effects (after treatment completion).

1.3.2 Study questions

1. How reliable is the cancer register and hospital episode statistics (HES) data in identifying type of treatment received, ethnic group and place of care?
2. Did hospital activity vary during and after completion of treatment for each major diagnostic group, taking into account follow-up duration? Did this relationship vary by patient demographic characteristics such as gender, ethnic group and/or socioeconomic status?
3. Was there variation in hospital activity by primary cancer and those individuals who relapsed compared to those who did not?
4. Did hospital activity rates vary among survivors compared with those who died during the study follow-up period? Was any variation in hospital activity explained by place of care?
5. Did the type of hospital admissions for the cancer cohort differ compared to the background population?
6. What were the most common causes of admission according to cancer type, age group and gender?

1.4 Thesis outline

In order to provide a comprehensive background for this thesis, Chapter 2 includes a detailed overview of children and TYAs with cancer, background information on the epidemiology of cancer in term of incidence, survival, type of treatment received, and type of morbidity. The specialist healthcare plan started earlier among young children (aged 0-14) compared with older children and young adults (aged 15-29). Based on that, the following section in Chapter 2 provides an assessment of the differences in managing cancer by age, children compared with young adults, by identifying the concept of specialist services, looking at when it was introduced, and what is meant by centralised services (Section 2.4). This section provides a detailed review of the current management of healthcare services for CYP with cancer in the UK. It explains the procedures and policies that were released to accommodate the provision, and the places where cancer survivors have been treated are introduced so as to consider the variation in managing cancer by different cancer types and age groups, which could directly impact hospital usage. Following that, a detailed review of the current knowledge on hospital activity amongst survivors of CYP cancer is provided in Chapter 3. Provides details of the materials and methods used in extracting data, preparing it for further analysis, and details the statistical analysis process. The results are then summarised in four chapters: an overview of the study population and cancer related clinical

characteristics (Chapter 5); Chapter 6 describes patterns of hospital admissions and length of stay during and after treatment completion, taking into account varied demographic and clinical characteristics such as age, gender, ethnicity, type of initial treatment and proportion of specialist care; Chapter 7 presents the result of multivariable analysis providing a summary of the factors that influence the hospitalisation rate after diagnosis with cancer for all cancers combined and separately by histological sub-types; while Chapter 8 is designed to assess the morbidity that leads to hospitalisation, starting by explaining the frequency of case specific admissions during and after treatment completion and the excess hospitalisations compared with the background population. Chapter 9 then discusses the key results of the thesis and compares them with the available literature. It provides a summary of the main results, in terms of the factors influencing hospital admissions and length of stay and the excess morbidity among the cancer cohort. The study's clinical implications, strengths, limitations and future work are also presented in Chapter 9.

Chapter 2 Epidemiology and Management of Healthcare Services

2.1 Introduction

This chapter includes a detailed overview of children and young people with cancer, alongside a discussion of the age boundary definitions and tumour classification schemes for CYP. Following this, the chapter provides detailed background information on the epidemiology of CYP cancer, including the incidence and survival by common cancer types, before giving an overview of the current management of healthcare services for children and TYAs with cancer in the UK.

2.2 Children and young people's cancer

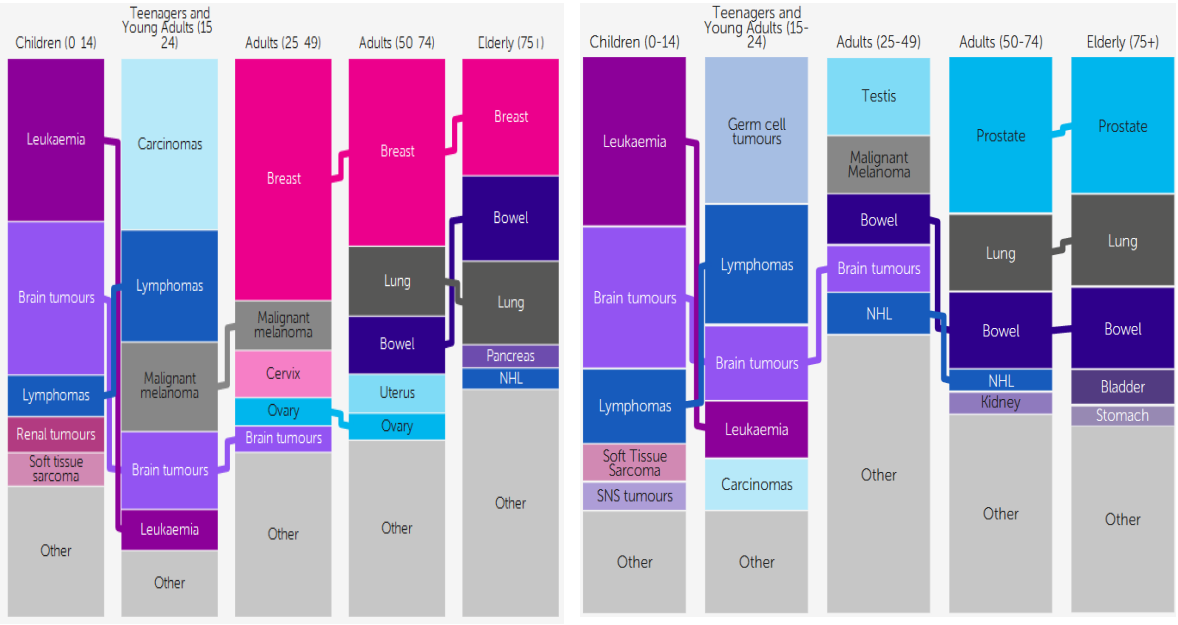
Despite cancer being relatively uncommon for CYP compared to adults, the incidence of cancer in younger people has steadily increased for most cancer types [30-32]. In addition, cancers among CYP can have devastating effects not only on those with cancer, but also on their families. Furthermore, cancer among CYP can have both short- and long-term implications as result of its treatment, and can reduce life expectancy. Moreover, cancer is one of the leading causes of death among children and TYAs [33].

Teenagers and young adults are in a transition period from childhood to adulthood. During this period, vital changes are taking place biologically, emotionally and socially. Carr et al.[2013] define the period of adolescence as:

> *"A time of search of identity and a period of rapid physical, social and emotional development, it is associated with significant remodelling of the neuroplastic adolescent brain"* Carr, et al. [2013]p.258[34].

Furthermore, TYAs diagnosed with cancer are in a critical phase, as they are often just starting their career paths. TYAs have distinctive types of cancer that differ morphologically from paediatric tumours and the tumours of older adults. TYAs can experience types of cancer that are predominant among younger children or older adults; these are embryonic tumours, such as Wilms' tumour, rhabdomyosarcoma and neuroblastoma that are considered 'late paediatric', since these are usually predominant among children aged less than five [35]. The other type is adult cancers, such as melanoma, thyroid and nasopharyngeal cancers that usually occur later in life but when they occur among TYAs are considered as 'early onset of adulthood' [35]. Additionally,

TYAs have a uniquely high frequency of tumours such as Ewing sarcomas, germ cell tumours and Hodgkin lymphoma, which are present to a high extent among the aforementioned group (Figure 1) [36]. TYAs diagnoses and clinical outcomes also differ from other groups. They have worse prognostic factors than children or adults. For example, TYAs with ALL have higher pseudodiploidity of the Philadelphia chromosome compared with children, which is usually related to poor outcomes [8]. TYAs on the other hand, fare better than children in tolerating complex treatments such as chemotherapy and radiotherapy [37].



Sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/age#heading-Two.

Figure 1:The five most common types of cancer among females (a) and males (b) diagnosed between 2009-2011. Data Sources [37]

2.2.1 Identifying age boundaries

There is variation when specifying TYA age boundaries to differentiate these from children. It seems arbitrary and varies depending on different perspectives, whether clinical or statistical; most of the UK research used 13 or 15 to 24 to specify young people and refers to them as teenagers and young adults [3, 8, 38-40]. In the US, 15-29 year-olds are included in adolescent studies, and 'young adult' studies in the US extend to those aged 35-39 years [2, 37, 41-43]. The common upper age limit for inclusion in paediatric epidemiological cancer research is 14 years; hence patients over the age of 14 are traditionally not included in childhood cancer research. The Office for National Statistics often uses 14 as the upper limit for childhood cancer statistics, which is driven from a statistical perspective [44]. However, from a clinical perspective, each diagnostic group has different age boundaries depending on the biology of the cancer. To avoid overlapping patients between childhood and adolescence, the age of 15 seems more

appropriate to serve as the lower limit for TYA cancer research. Patients aged 25-29 were included in teenage studies in the US [11]; however, this age group could have different frequencies of cancer compared with younger groups, and are usually treated using adult protocols in adult settings. Therefore, patients from this age group could reveal varied hospital activity because they received care in different settings, which could more accurately reflect adult activity patterns. Due to the dearth of knowledge regarding patients under the age of 30, in terms of incidence, survival, and the use of hospital activity, the effect of place of care and type of treatment (taking into account the length of treatment) on patterns of hospital activity, the current project addressed this lack of knowledge. More importantly, it took advantage of the availability of information among survivors aged up to 30 from the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) that was used to extract the study population (details included in Chapter 4, Section 4.6.1).

2.2.2 Cancer classification schemes

Three classification schemes were commonly used to classify cancer; the International Classification of Disease-Oncology (ICD-O) [45], the International Classification of Childhood Cancer (ICCC) [46], and the Birch Classification [38]. These were made to facilitate and provide a more standardised comparison of the types of cancer, both nationally and internationally.

Tumours occurring in CYP differ significantly from the more common adult cancers in terms of their biology and presentation. ICD-10 coding is used to classify adult cancers using primary site (topography), such as lung carcinoma and other epithelial cell cancers. A more helpful classification for CYP tumours is that based on ICD-O coding as it includes information on the morphological features of tumours as well the topography. However, carcinomas from non-epithelial cells, which are rare among adults but have a high incidence in TYAs, are not recorded in detail in the ICD-O. Childhood cancer usually originates from specific types of cells or histological types, rather than specific organs. The types of cancer that were classified in this scheme were mainly related to embryonic tumours, which commonly occur among children but to a lower extent among TYAs. The ICCC was not developed specifically for TYA cancers. Therefore, when TYA cancers were classified according to the ICCC scheme, a high percentage of cases were classified as “unspecified” [47]. Another classification scheme designed for TYAs was the Birch [38] TYA scheme, which is similar to ICCC in allocating cancer type using morphological codes, however includes additional groups to allocate cancers that are common among TYAs, such as melanoma and carcinoma. Although the Birch classification was found to be better suited to classify the TYA cancer diagnostic group

[48], it was not adapted for paediatric cancers, as melanomas and carcinomas do not occur among children.

Nevertheless, in this thesis the hospital activity pattern were analysed for children and TYA. Hence, it was essential to have one scheme for both children and TYAs to provide comparable data. It would be ideal to have separate classification schemes for each age group, however, ICCC was found to properly classify cancer among TYA. The variation in cancer outcomes among children and young people was assessed before and in classifying the TYA cancer, two classification schemes were used and compared: Birch and ICCC-3 [49]. In their study, it was found that ICCC only allocated 0.1% of cases as unknown, while 2% of cases were left with an unknown cancer type using the Birch classification scheme, additionally more cases were identified as 'others' using Birch compared with ICCC [49]. The current thesis used the same data sources and similar data catchments as the aforementioned studies, hence the use of ICCC to classify cancer types for children and TYA was reliable among the study setting, in addition to facilitating internal comparison between cancer types and the study age group [49].

2.3 Epidemiology of cancer

2.3.1 Cancer incidence

One out of 500 children develop cancer before the age of 14 [36]. While in the period 2009 to 2011, there were around 4,556 cancer diagnoses per 100,000 persons aged 15-24 in the UK [36]. In the UK, only 1% of the total cancer cases were diagnosed at the age of 15-29, although this increased by 0.5% from 2006 [21, 36]. Additionally, TYAs are 50% more likely to be diagnosed with cancer than children under the age of 15 [36]. This pattern is similar in the USA [37, 50]. In 2006, TYAs accounted for almost 2% of the total cancer incidence in the USA [37], which is higher than in the UK [51].

Cancer incidence among CYP varies according to diagnostic type. Among patients under the age of 15, leukaemia and brain tumours are the most common types of cancer and account for almost half of the incidences, followed by lymphomas, which account for 10% of the total cases (Figure 2) [52].

Lymphomas are the predominant cancer among TYAs aged 15-24. In the UK, the standardised incidence rate of lymphoma was 421.7 per million person-years from 1995-2009, followed by carcinoma and germ cell cancers, where the incidence rates were 392.5 and 310.9 per million person-years, respectively. Leukaemia was the sixth most common type of cancer, just after cancers of the CNS and melanoma, although it had the highest related cause of death in this age group [36]. In the USA, similar types of cancer occurred among TYAs, with lymphomas (Hodgkin lymphoma - HL) being the

leading type of cancer (16%), followed by germ cell and CNS cancers at 15% and 10%, respectively [50].

2.3.2 Survival

Cancer accounts for 10% of the total number of deaths among children older than one year old [18]. As a result of breakthroughs and improvements in treatment, including clinical trials, the survival rate of children has shown significant improvement, rising from 30% at the end of the 1960s to 82% at the beginning of the 21st century [53]. However, the range of improvement gradually decreased, the biggest was between 1961/70 and 1981/90, lower improvement was noticed between 1981/90 and 1991/2000 and no improvement in 1991/2000 and 2001/10 [54]. TYAs also had advantages resulting from enhancements in treatment protocols, especially from 1998-2009, as evidenced by the fact that the total five-year survival rate reached 84% in the North of England [55]. Overall, the survival of patients with leukaemia, lymphoma, Ewing sarcoma and CNS cancers has improved over time, although it was worse in TYAs aged 15-24 than in children under 15 [55]. In 2009, Pearce suggested that this disadvantage in outcomes is related to the rare frequency of cancers, the distinctive biology of cancer, limited entrance to clinical trials, late prognosis, late referrals and a lack of standardised treatment [21].

Over the last 40 years (1968 to 2008), the five-year survival rate increased from 46% to 84% in the North of England, as evidenced by population-based registers [55]. This improvement could be due to the improvement in treatment in the 20th century, in particular for acute myeloid leukaemia (AML) in males, as their survival was not statistically different from females from 1998 to 2009 compared with earlier periods [55].

Lymphomas have the highest survival rate, reaching 89% in 2005; it increased by 5% from 1991 to 2005 among TYAs. Leukaemia had the poorest survival rate of only 49% in 1991, although this increased to 62% in 2005 [36]. The TYA survival rate markedly improved in 2009, reaching 84% overall, and CNS, germ cell tumours and melanoma had the highest survival rate (94%, 96% and 100%, respectively). In particular, AML and Ewing sarcoma showed the largest treatment improvements, as survival increased from 0% in 1968 to about 50% in 2009 [55].

2.3.3 Epidemiological risk factors

2.3.3.1 Age

Teenagers and young adults had a better prognosis than children, and the survival rate between 2002 and 2006 was better than for children and older adults, having 82.5% five-year relative survival compared to 82.0% and 65.9% among children younger than 15 years and adults older than 40 years, respectively [43]. However, the percentage of improvement per year was lower than for children with 58% compared to 52% among

children and TYA, respectively [43]. From 2002-2006, the survival rate for TYAs aged 15-29 was significantly better than adults aged 40-49 in the USA, especially for leukaemia, lymphomas and non-gonadal germ cell cancers [51]. Although they found better survival rates among TYAs younger than 40 years old, than adults aged above 40, they found that other non-specific types of leukaemia had poorer survival rates among younger groups [51]. Additionally, breast cancer among TYAs had worse outcomes, with an 80% five-year survival rate among patients aged 15-29 compared with 88% in patients aged 40-49 [51].

2.3.3.2 Gender

Cancer is more common among males, except for melanomas and carcinomas, which are more common in females [36]. From 1968 to 2009, females had significantly better survival rates than males. Additionally, they were 17% less likely to be at risk of death, after adjusting for age, period of diagnosis and deprivation, than males [55].

2.3.3.3 Ethnicity and socioeconomic status

Survival among TYAs aged 15-24 suffering from haematological cancers (leukaemia and lymphomas) was not related to economic deprivation. In contrast, childhood cancer was related to socioeconomic status, as childhood leukaemia was negatively associated with deprivation, with the most affluent people having a greater risk of leukaemia [56]. In previous studies it was found that TYAs aged 15-25, in general, had better survival in the most affluent areas [55]. However, they did not take into account cancer stage or ethnicity, which are usually correlated with deprivation. In their study, non-Hodgkin lymphoma (NH) survival was better in the most affluent areas, while CNS cancer survival was worse in the most affluent areas [55]. These differences show that cancers in TYAs have varied biological causes between diagnostic groups and other age groups, which requires further research. Furthermore, it could be related to the location of specialised healthcare services, as CNS cancer specialist care in Northern England is located closest to less affluent survivors [55].

Several studies found correlations between cancer incidence and ethnicity in Europe and the UK [57, 58]. South Asians had higher cancer incidence for the majority of cancers than non-South Asians in the UK [59-61]. Although in Yorkshire the incidence of cancer among CYP was not significantly different between South Asians and non-South Asians, it was expected that South Asians would have approximately threefold the risk of cancer compared with non-South Asians in the future (2005-2020) [62]. The USA similarly found variations of cancer incidence by ethnicity, the incidence of leukaemia was lower among black young people compared with white young people.

2.3.4 Evolving cancer treatment

There has been evolution in the management of cancer treatment, especially among haematological tumours such as leukaemia and lymphoma, however, limited development is observed among solid tumours such as CNS tumours, neuroblastomas and bone tumours [42]. Emphasis is now on ensuring that optimal therapy is administered at the minimum level of intensity to cure the patient, whilst reducing the risk of any side effects and late effects of treatment. However, the treatment among TYAs was not evolving at the same speed as that for children and older adults. TYAs have experienced slower and more stable improvements in survival compared with children which could be partly due to reduced availability of clinical trials [6, 63]. TYAs have experienced slower and more stable improvements in survival compared with children which could be partly due to reduced availability of clinical trials [64]. Furthermore, TYAs may be more likely to experience longer time to diagnosis due to personal and/or professional delays, and perhaps be less compliant with treatment protocols than younger children [65]. Clinical trials were used as a representative for improvements in cancer treatment, and TYA aged 15-29 had the lowest percentage of enrolment in clinical trials [30, 66], which also decreased each year compared with older adults whose enrolment rate improved each year [66]. In developed countries, such as Australia, the USA and the UK the accrual rate of TYA was lower than for younger children [63]. In the USA in 2000, the *Children's Oncology Group Adolescent and Yong Adult Committee* was established, as a result there was an increase in clinical trials opened for TYAs in the period 2003 to 2005, thus an increase the involvement of TYAs in clinical trials [42]. Similarly, in the UK in 2005 there was encouragement for the availability of age specialist units for young people (more detail in Section 2.4), as these units were believed to increase the accrual rate among TYAs in clinical trials, hence improve treatment and quality of life among survivors [67].

2.3.5 Cancer related morbidity

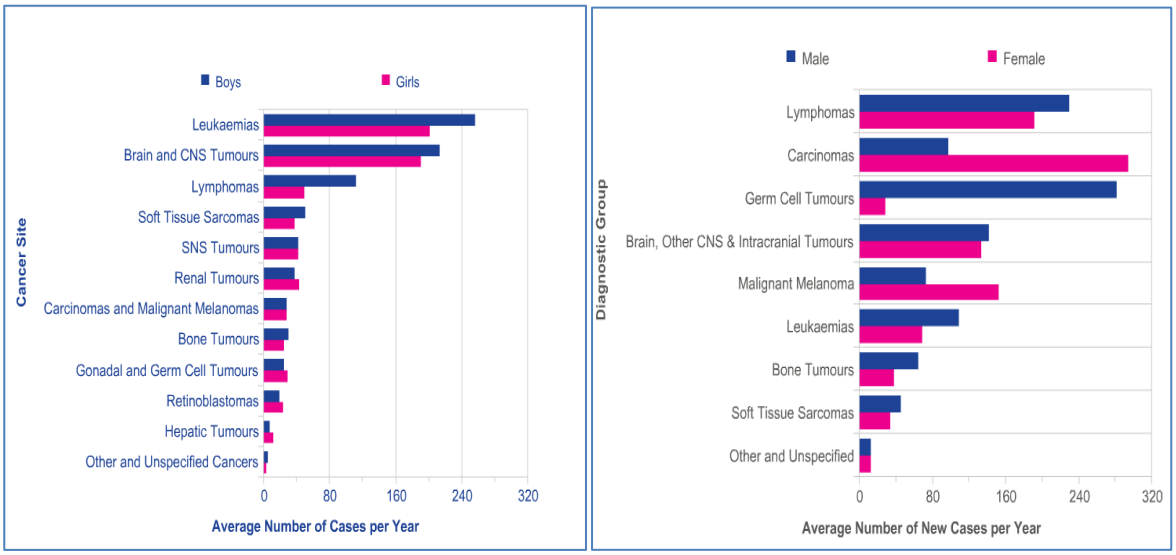
Children and young people with cancer might suffer from complications shortly after diagnosis or in the long term after completing treatment. During the treatment period, they might be admitted for infections, organ toxicity, malnutrition, nausea and bleeding, and these rates were higher among TYA than children [42, 50, 68]. Due to the increased survival pool among CYP, as presented earlier, in the UK there is an annual 3% increase in the number of survivors on average [69]. This increases concerns about the well-being of those survivors, not only in terms of survival rate, but also in terms of long-term well-being by reducing treatment side effects. Different types of morbidity that survivors experience in the long term, i.e. in the five years following the date of diagnosis, include mental disorders such as stress and anxiety, or cognitive disorders [25, 70], cardiovascular diseases [71], recurrent neoplasms [24], death [28], endocrine diseases

[72], and loss of fertility [73]. Survivors were at higher risk of autoimmune diseases during the 1-year survival rate compared with the background population was 1.4, 95% CI: 1.3-1.5) [74]. These types of morbidity were linked previously to the type of treatment delivered and its toxifying elements, such as anthracycline treatment that was directly related to an increased risk of cardiovascular consequences, and radiotherapy which was related to an increased risk of infertility [73]. These highlight that CYP are in continuous need for health services to cope with their diseases; the type of morbidity cases that might be experienced relate to the type of cancer as explained in the following sections.

2.3.6 Leukaemia

2.3.6.1 Incidence rate

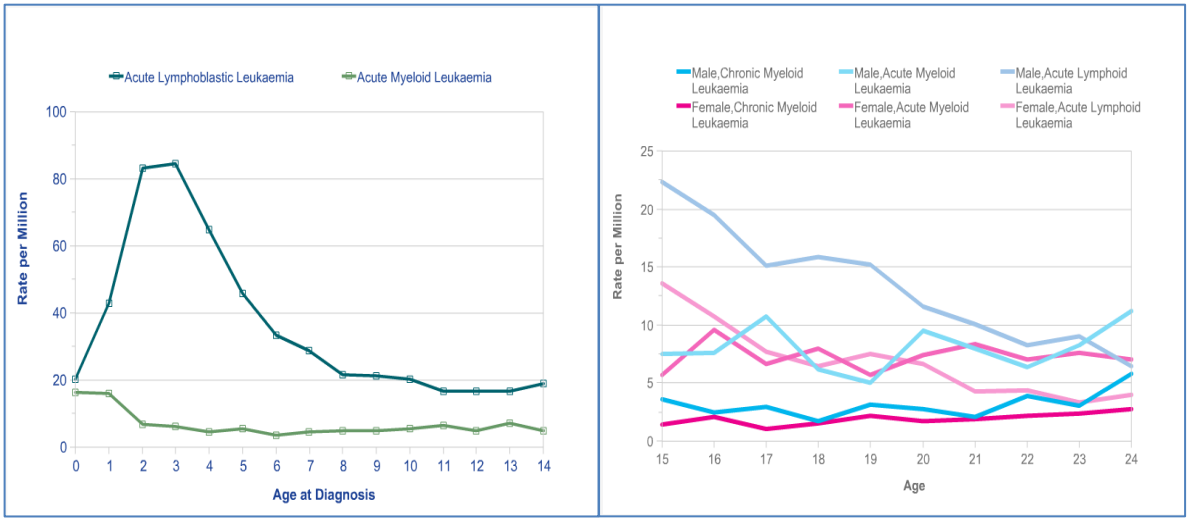
Leukaemia is the most common type of cancer among children under the age of 14, and it falls within the six most important diagnostic groups among TYAs (Figure 2). In both age groups, acute lymphoid leukaemia (ALL) was more predominant than acute myeloid leukaemia (AML), as presented in Figure 3, and was higher among young children than TYAs, peaking at the age of two to three [39, 75]. In the United States, leukaemia is the leading cause of cancer deaths among males younger than 39, and it was the second and third leading cause of death among young girls and women, respectively [76].



(a) **(b)**

Sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-Three

Figure 2: Incidences of common types of cancer among children aged 0-14 (a) and 15-24 (b) (2006-2009) in the UK. Data Sources [38]



(a) **(b)**

sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/incidence#heading-Four

http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-One

Figure 3: The average annual leukaemia incidence in million person-years in the UK, (a) children aged 0-14 and (b) TYAs aged 15-24.Data Sources: [41,74]

2.3.6.2 Evolving cancer treatment

Leukaemia is one of the cancer types that has seen rapid improvements in treatment strategies, due to the availability of a range of clinical trials, in relation to the relatively high incidence among CYP. ALL was the predominant diagnostic group among children; hence it has been the focus of several clinical trials in the UK. The UKALL X trial, which included patients under the age of 15, added two courses of five-day intensive treatment for five and 20 weeks during remission, and, as a result, progress in improvement was attained, as the event-free survival rate reached 60%. The intensified treatment has progressed, though it still includes a similar age range (<15). From 1990-1997, the UKALL XI trial introduced a third intensive five-day treatment at 38 weeks. However, the intended improvement was not reached, as the event-free survival was unchanged. Thus, the overall survival improved from 73% in 1989 to 80% in 1997. This intensified protocol increased the toxicity in short- and long-term survivors, especially among low-risk patients. Because it included patients with all stages of cancer, the scope of improvement in terms of the rate of relapse was not described [29, 77]. The UKALL 97/99 trial limited the usage of radiation therapy to prevent the occurrence of CNS related diseases. These improvements produced an advantage in patient outcomes; it is now rare that a patient has defects in puberty or development as a result of cranial radiation [78]. One of the

strategies for ALL trials is that all patients need to be treated for at least a two-year maintenance period (18 months for girls and 30 months for boys) [53]. Patients may need up to three years of hospital care [79]. TYAs were found to perform better when treated with the children's protocol, hence paediatric trials increased their upper age limit to include young adults, and the UKALL trials have included patients up to 18 years old since UKALL97/99 and UKALL 2003. UKALL 2003 recruited patients from 2003 to 2011, and the upper age limit increased to include patients up to 20 years of age in 2006 and 24 years in 2007 [80]. Starting from the UKALL XI trial, patients received their treatment at home rather than in hospital. This change in the type of administration of chemotherapy to children up to 18 years of age was strongly related to patient social class. Currently, treatment for ALL in comparison with other diagnostic groups among children has been prolonged to three years [81]. Hence, it is important to understand the variation in treatment periods for each diagnostic group, because it could affect the pattern of using hospital resources, although this has not been studied before. Not only the therapeutic protocol, but also the prognostic process, has modified how patients are categorised. For example, patient categorisation now depends on the specific cytogenetic abnormalities and other characteristics of leukaemia cells, rather than the age of a child or the counts of white blood cells [82].

AML has also experienced an improvement in treatment plans, as evidenced by an increase in the number of treatment doses [82]. In the US, the improvement in AML treatments was directed not only by increasing the intensification of post-consolidation therapy, but also by providing supportive care to ensure proper administration of therapy [82]. Stem cell transplantation contributed to major improvements in the outcome of AML by using allogeneic transplantation that decreased the rate of death among patients with transplantation [82].

2.3.6.3 Survival

Leukaemia childhood survival has improved over time; it increased from 75% in 1991-1995 to 83% in 2001-2005 in the UK, and among TYAs it improved from 49.2% to 62.1% during the same period [31, 32]. The differences in survival could be related to the different biology of tumours among TYAs as opposed to children, and the noted improvement in prognosis and treatment was better addressed among children than TYAs. Indeed, the outcome differences highlight the significant improvement that has been made in the long history of treating childhood cancers. The survival rate for ALL significantly improved from 61% to 88.5% among US children from 1975 to 2002. Likewise, survival of AML massively improved from less than 20% to 58% and to 40% among children and TYAs (aged 15-19) respectively [82].

2.3.6.4 Cancer related morbidity

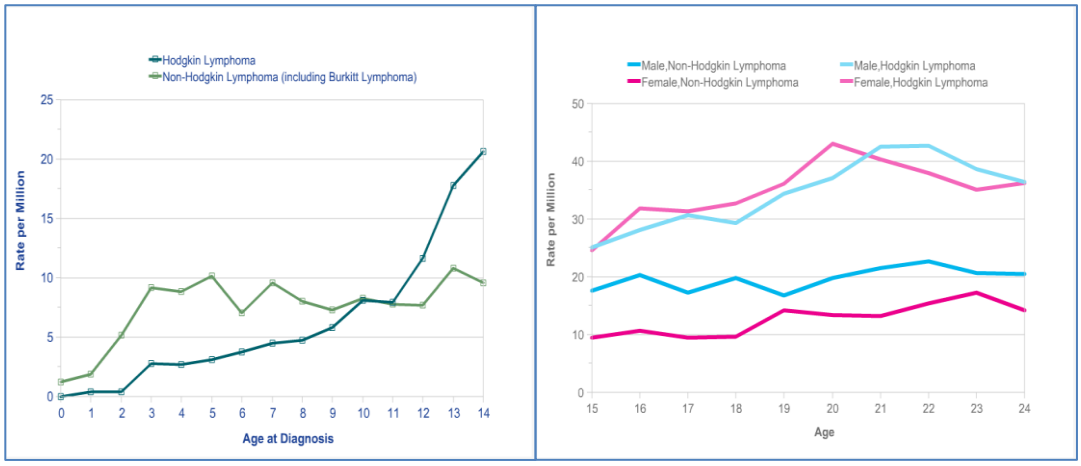
Leukaemia survivors were at increased risk of recurrent malignancy, cardiovascular diseases, infertility, autoimmune disease and deficiency in growth development [33, 83-87]. Endocrine disorders were higher among CYP with leukaemia compared with other cancer types; these rely on exposure to local radiation and chemotherapy [72]. The risk of recurrent malignancy among leukaemia survivors was higher among survivors that had radiation compared with survivors that did not receive radiotherapy [83]. The causes of infertility were related to the type of chemotherapy substance, an alkylating agent was directly related to decreasing the reproductive life among male and female survivors compared with their siblings [85, 86]. ALL survivors suffered higher levels of chronic conditions (odd ratio= 3.6: 95%CI: 3.0-4.5) and life-threating conditions (odd ratio= 3.6: 95%CI: 3.0-4.5) than their siblings [88]. The risk of death as a result of cancer was higher among leukaemia CYP survivors than other cancer types [27].

2.3.7 Lymphoma

2.3.7.1 Incidence

Lymphomas are more common among TYAs than children. It is the leading type of cancer among TYAs and the third most common type of cancer among children; the incidence rate is 220 and 100 per one million person-years, respectively (Figure 2).

Non-Hodgkin lymphoma (NHL) is predominant among children aged between 0 and 10, while it is less common among older children and young adults aged 11 to 24 (Figure 4). Hodgkin lymphoma (HL), on the other hand, is more common in older children, peaking at the age of 20 to 21 and reaching 40 per million person-years.



(a) **(b)**

sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/incidence#heading-Six http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-One

Figure 4:The average annual lymphoma incidence in million person-years in the UK, (a) children aged 0-14 and (b) TYAs aged 15-24.Data Sources [41,74]

2.3.7.2 Evolving cancer treatment

It is better to explain the change in treatment depending on specific diagnostic sub-groups, because each sub-group has a specific prognosis and treatment regime. NHL survival has dramatically improved due to adjustments in treatment plans. It is worth noting that different strategies have been used for treating lymphoblastic lymphoma and non-lymphoblastic lymphoma. High doses of methotrexate were prescribed to patients with B-cell NHL (non-lymphoblastic lymphoma) and provided better outcomes, while for lymphoblastic lymphoma, the ALL strategy was administered [82]. One of the changes in HL was an increase in the intensity of the treatment, by administering the radiotherapy around the lymphoid which resulted in improved survival rates [89]. The HL trial focused on minimising treatment-related morbidity and maintaining the survival rate, as survival rate currently exceeds 90% [82].

2.3.7.3 Survival

Children and TYAs have experienced improvements in overall survival from 83% to 87%, and 84% to 89% from 1991-1995 to 2001-2005 respectively in the UK [31, 32]. The transit of improvement among childhood HL occurred in 1980/90, with no significant improvement thereafter. While children with NHL saw improvement from 72.2% in 1981/90 to 88.7% in 2001/10 [54]. The distinction in the trend of improvement could be

justified by the fact that NHL, as the most predominant lymphoma diagnostic group among children, was the focus of clinical trials and treatments and went through continuous improvements, which successfully increased the survival rate from 45% to 88% in the US [82]. Another reason is that childhood HL had already reached satisfactory improvements as it reached 92.3% in 1991/2000. TYA with HL had a poorer survival rate from HL, while it was better than for older adults [43]. TYA with NHL saw faster improvements each year with 4.92% annual change compared with 0.67% among children; however the survival rate is higher among children than TYA [43]. TYA with HL, on the other hand, lagged behind the survival rates among younger children and older adults [90].

2.3.7.4 Cancer related morbidity

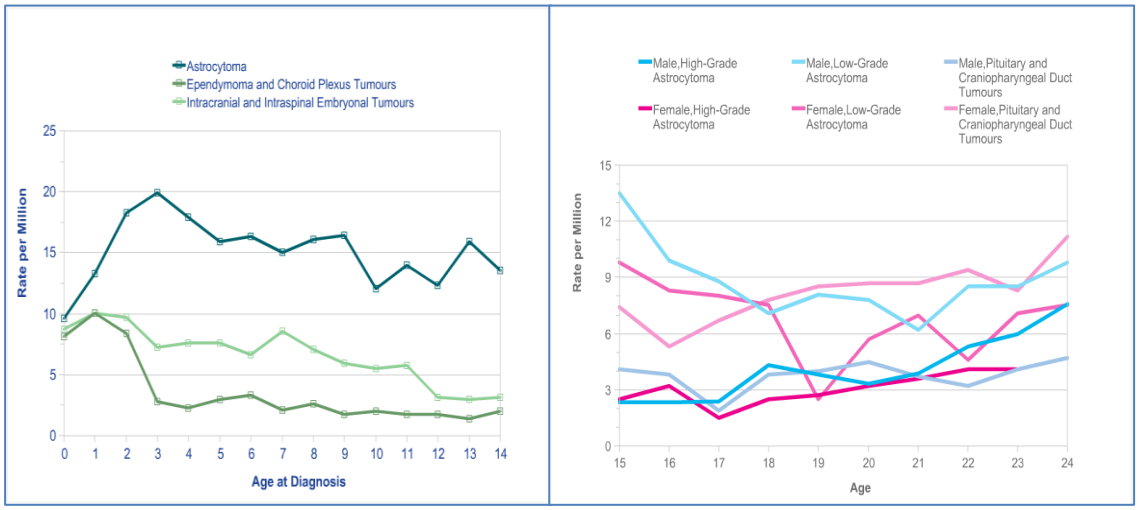
As a result of the changes in the treatment intensity of HL, survivors were at high risk of autoimmune diseases, mental disorders, secondary malignancy and cardiovascular disease [25, 89, 91, 92]. The risk of mortality among HL was higher among older children aged 15-21 than younger children aged 10 and younger [92]. HL and NHL were at high risk of chronic disease compared with their siblings, it was higher among the HL group than the NHL group [93].

2.3.8 CNS tumours

2.3.8.1 Incidence

CNS tumours are the second most common type of cancer among children under 14 for both genders, and the third and fourth most common type among male and female TYAs, respectively (Figure 2). In particular, note that they are the second leading cause of cancer deaths among CYP in the US (aged <39) [76].

The average incidence rate of CNS cancers among children is 200 per million person-years and 130 per million person-years among TYAs in the UK. There are variations in the incidences of CNS cancers among specific diagnostic groups between children and TYAs. Astrocytoma has the highest incidence among children, followed by intracranial tumours and ependymomas (Figure 5). Among TYAs (aged 15-24), the specific diagnostic groups of CNS cancers vary by gender, as astrocytomas were more common in males than females, whereas intracranial tumours more common in females [39].



(a) **(b)**

Sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/incidence#heading-Six
http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-One

Figure 5: The average annual incidences of brain tumours in million person-years in the UK, (a) children aged 0-14 and (b) TYAs aged 15-24.Data Sources: [41,74]

2.3.8.2 Evolving cancer treatment

CNS tumours have received a decreased intensity of treatment (reduced length of therapy and reduced radiation dose) specifically tailored to reduce late effects of treatment and to improve the survival rate [82]. This is especially true for children less than 14 years old, where exposure to radiation is delayed or removed from the treatment plan. This group experienced greater improvement and lower long-term morbidity as a result of these treatment changes [82]. However, children with medulloblastoma / PENT experienced an increase in treatment intensity, by introducing chemotherapy before and after receiving radiotherapy, which resulted in improving disease free survival rates, as found in several international trials such as *North American Pediatric Oncology Group* and *Children's Cancer Group* (CCG), and the *European International Society of Paediatric Oncology* (SIOP) [94]. CNS survivors were treated with surgery, radiotherapy and chemotherapy, where the radiotherapy was the most effective treatment. In the latest trials, the intensity of radiotherapy was managed based on the age of the patient and the biology of the tumour, children younger than three were usually not initially treated with radiotherapy due to its negative effect on the developing nervous system [95]. Additionally, increasing the intensity of chemotherapy and reducing the doses of radiotherapy among children resulted in improvements in event-free survival rates [95]. Less is known on the improvement in treatment among TYAs, however, among the

limited research it was found that the survival rates were better when they were treated with chemotherapy before and after radiotherapy, suggesting favourable outcomes for the use of chemotherapy among older groups [95].

2.3.8.3 Survival

Among children aged younger than 15, the five-year survival rate of CNS had significantly improved from 70.1% in 1981/90 to 88.7% in 2001/10 [54]. From 2001-2005 the survival rate of CNS was better among TYAs than children and older adults, the five-year survival rate was 93% among TYAs, while it was 86% among children [90]. However, the pattern was not consistent among CNS detailed histological subtypes, ependymoma was better among TYAs, having a 96% survival rate, while it was 69.8% among children [43]. The survival rate of medulloblastoma was better among children than TYAs with 75.6% among children and 65.4% among TYA [43]. In 2005, the overall survival rate for patients aged 15-24 reached 81.1% [31]. In the US, children less than four years old saw the best improvement, reaching 73.1%, whereas it was 53.1% in the early seventies, that was explained by the reduction in systematic chemotherapy, particularly for non-medulloblastoma [96].

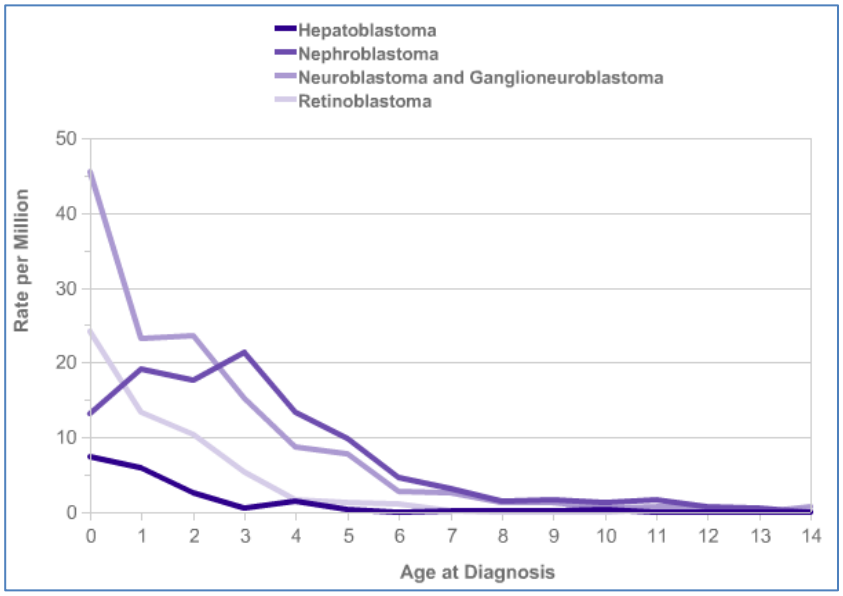
2.3.8.4 Cancer related morbidity

CNS survivors were at risk of chronic illness compared with their siblings, with a relative rate of 7.1 (95% CI 6.3-8.2) [93]. More precisely, they were at highest risk of organic memory and brain dysfunctions compared with other cancer types, with an odd ratio of 24.0 (95%CI: 13.4-43.2) [25]. The late psychiatrics morbidity was higher among children with CNS than TYAs [25]. Child, teenage and young adult CNS survivors in general suffer from mental disorders, and more use of antidepressants with cancer [97-100]. However, by assessing hospital admissions among long-term survivors it was found that CYP were at lower risk of admission due to serious psychological disorders compared with the background population [101]. The management of treatment similarly could influence the burden of health, TYA CNS survivors that were managed in specialist centres were likely to have better survival rates than cases with limited specialist care [8]. The type of short- and long-term treatment effects varied by type of initial treatment; cases treated with radiotherapy were at risk of nausea, increased sleepiness and anorexia within two to six weeks after treatment, and the long-term effects might be reflected in reduced intelligence, especially among children younger than seven, and cerebrovascular disease [95].

2.3.9 Neuroblastoma

2.3.9.1 Incidence

A neuroblastoma is more common among children and is classified as an embryonic tumour. The annual incidence of neuroblastoma among children aged less than 15 was 11.6 per million person-years [68]. It was more common among children younger than four years of age than older children (Figure 6) [36, 75]. A 27.4 neuroblastoma incidence per million person-years occurred among children younger than five years, and it ranged between 0.5 and 2.6 per million among older children aged 5-19 years [50].



Sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/incidence#heading-Nine

Figure 6:The average annual incidences of neuroblastoma in million person-years in the UK among children aged 0-14.Data Sources: [36]

2.3.9.2 Evolving cancer treatment

The improvement in treatment was more favourable among high risk cases where they were exposed to high doses of chemotherapy and the use of autologous stem cell transplant [82]. However in more recent data, infants and children had better survival when they were treated with less intensified treatment, including lower doses of chemotherapy [102, 103].

2.3.9.3 Survival

The rate of survival was stable among infants, however the survival rate reached 95% in 1999/2001, and that was better than for older children where the survival rate was 65% [82]. This is similar to data extracted from the *International Neuroblastoma Risk Group* (INRG), based on diagnoses from North America, Europe and Japan, as the survival rate was poorer among the older group, and that was justified by the lack of centralised treatment among TYAs [104]. The difference in survival rate was related to the prognosis of the tumour as an infant, which had more favourable biology of disease than older children [82]. The survival rate of neuroblastoma among children improved from 57.0 to

66.5 from 1981/1990 to 1991/2000, and reached 68.2 in 2001/10, however, with no significant improvement in 2001-2010 [54].

2.3.9.4 Cancer related morbidity

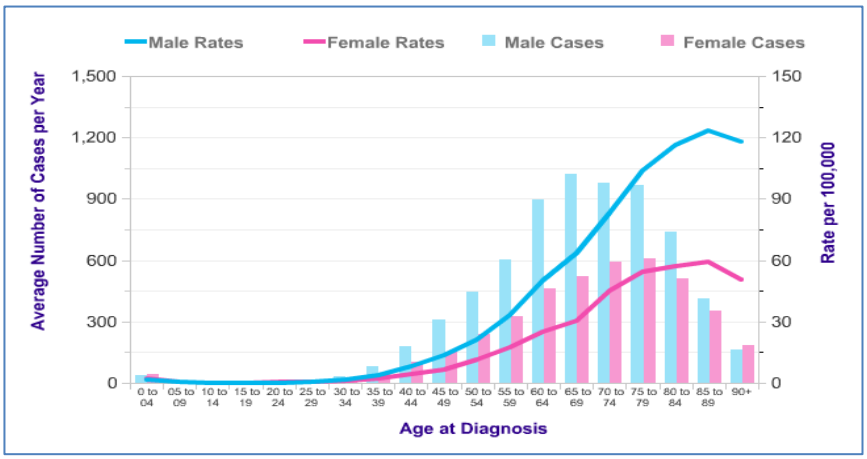
Survivors of childhood neuroblastoma were at higher risk of depression than a comparison group [25, 105], however these might be for older children, as infants were less likely to be treated with cytotoxic chemotherapy than the older group [82]. They were at high risk of endocrine diseases such as diabetes, hearing loss, and ovarian insufficiency after having a stem cell transplant, these long-term illness mainly occurred in the high risk group treated with stem cell transplant [106]. Limited information was available on the type of morbidity occurring after treatment completion for all cases with neuroblastoma among TYAs.

2.3.10 Renal tumours

2.3.10.1 Incidence

Wilms' tumours are usually classified under embryonic tumours, and constitute the majority of renal tumours among children less than 14 years of age [82]. Among children younger than four, 90% of total kidney tumours are Wilms' [5]. These types of tumours are common among children under the age of five, and less common among older children.

The incidence of renal tumours that merged from the renal cells carcinoma increased by age (Figure 7), this type of tumour is more commonly found among older adults [107]. The incidence significantly increased over time from 2000 to 2011 among TYAs aged 15-39 years, compared to older adults [41]. This increase relates to improvements in diagnosis of renal tumours and successfully diagnosing tumours at an early stage [30].



Sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/incidence#heading-One

Figure 7: The average annual incidences of renal tumours in 100,000 person-years in the UK. Data Sources: [38]

2.3.10.2 Evolving cancer treatment

The greatest improvements were in the 1980s, during which a new regime was introduced (doxorubicin) to high-risk patients [82]. The majority of Wilms' trials focused on avoiding treatment-related morbidity [82, 108]. Hence, this type of cancer could see reduced hospital visits due to complications, in comparison with other diagnostic groups. The period of treatment and its intensity was reduced in the 90s, however, this did not reduce the favourable outcomes [82]. Recent trials on Wilms' tumours in the UK found that patients treated with chemotherapy prior to surgery had better outcomes than patients who were immediately treated with surgery. The improvement, although not appearing in the survival rate, reduced the use of radiotherapy and intensive chemotherapy among patients with preoperative chemotherapy [109].

2.3.10.3 Survival

Early in the 1970s, children with renal tumours cases were treated using vincristine and dactinomycin in combination with surgery, which resulted in a 70% survival rate [82]. In the US, during the 15-year period from 1987 to 2002, the survival rate showed little or no improvement among children with renal tumours, however, the rate was above 90%, which could be considered a favourable outcome [54, 82]. Among cases aged 17-55 the survival rate of Wilms' tumours in an advanced stage was worse in the older group than in children [110]. This represents the variation in the renal survivor pool by age, and stage. TYAs had relatively better survival rates than older adults with 85.1% and 71.8% respectively, however, they saw significantly slower improvements than older adults by year [43].

2.3.10.4 Cancer related morbidity

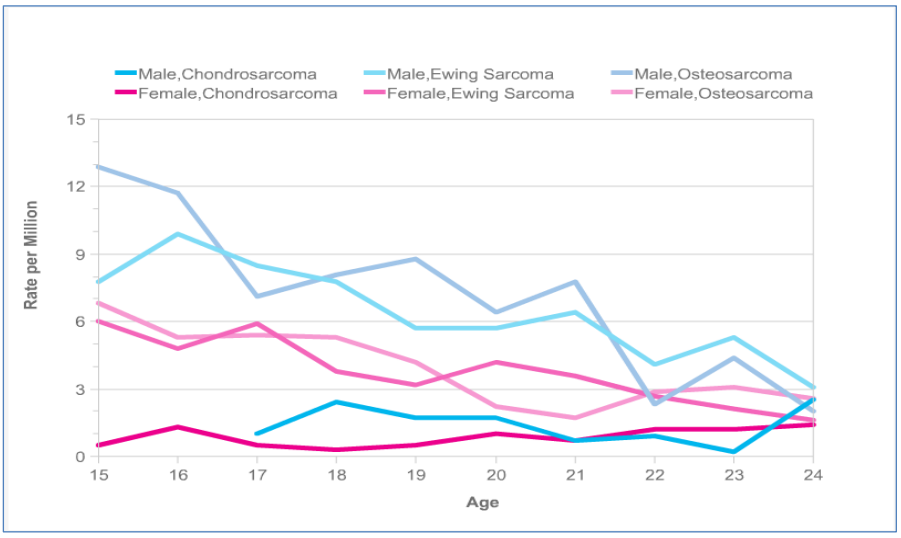
Children and young people with renal tumours were significantly at higher risk of autoimmune diseases compared with the background population after being diagnosed with cancer [87]. Survivors of renal tumours were at lower risk of being hospitalised, hence low morbidity in long-term survivors, this is linked to the nature of the treatment, as renal tumours are treated with lower toxicity treatments compared with other cancer types [15]. Childhood renal survivors had the highest risk of diabetes compared with other cancer types, the relative risk of hospitalisation due to diabetes was 2.9 (95% CI: 2.1-4.1) compared with background population [87].

2.3.11 Bone tumours

2.3.11.1 Incidence

The average annual incidence of bone tumours in TYAs is almost double that in children, 40 and 20 per million person-years, respectively (Figure 8) [111]. Osteosarcoma is the most common bone cancer among children, followed by Ewing sarcoma. Both in females

and males aged 14-24, Ewing sarcoma and osteosarcoma are more common than chondrosarcoma (Figure 8). Ewing sarcoma is more common among TYAs than young children [5].



Sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/teenagers-and-young-adults-cancers/incidence#heading-One.

Figure 8:The average annual incidences of bone tumours in million person-years among TYAs aged 15-24 in the UK. Data Sources: [112]

2.3.11.2 Evolving cancer treatment

Bone tumours, although not dramatically changed, have experienced some alterations regarding treatments among both children and adolescents, which successfully improved their survival rates [82]. The survival of osteosarcoma in the UK was worse than in Germany, where the variation seems due to the administration of multidrug chemotherapy in the 1980s [112]. However, recently the treatments have been similar among both countries after collaborations with the *European and American Osteosarcoma Study Group* (EURAMOS) that aim to improve long-term survival of bone tumours, as the survival rate among bone tumour survivors saw no significant improvement [113]. Bone tumours are treated with aggressive chemotherapy including 12-15 courses that might last from 8-12 months, which is followed by local surgery for tumour extraction [114].

2.3.11.3 Survival

The overall survival rate slightly improved, but was generally stable from 1991 to 2005, especially among children, in which the five-year survival rate stabilised at 61% [32]. The survival rate for osteosarcoma improved from 2003 to 2009, reaching 71% compared with 45% in the period 1975-79 [5]. The survival rate for Ewing sarcoma also increased from 42% to 72% during the same study period [5]. TYAs had a poorer survival rate compared with children and older adults [43, 54]

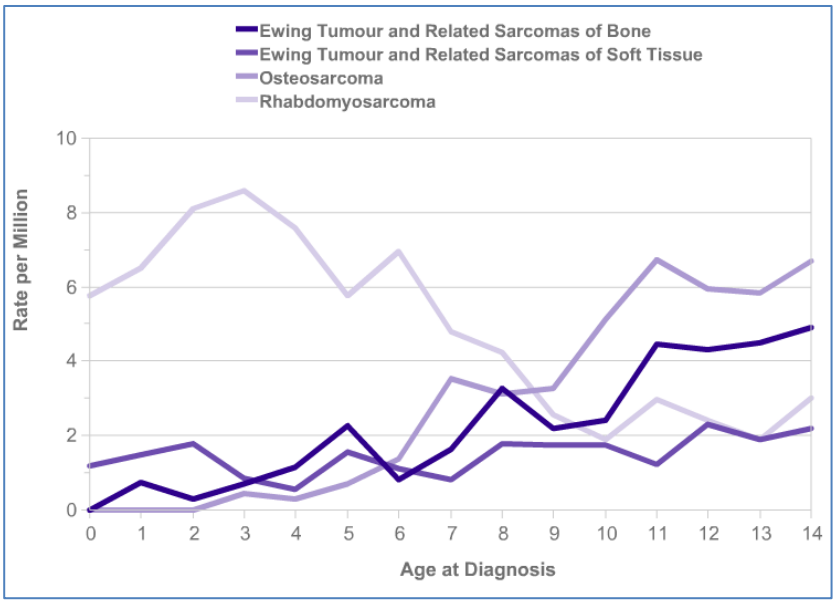
2.3.11.4 Cancer outcome and related morbidity

Bone tumour survivors have a higher risk of chronic conditions compared with their siblings; and higher than other cancer types [93]. In addition to the risk of early recurrent malignancy, cardiopulmonary disease and mortality, bone tumour survivors suffer from physical and orthopaedic conditions [24, 115-118]. However, this research was based on questionnaires, hence subject to selectivity and recall bias.

2.3.12 Soft tissue sarcoma (STS)

2.3.12.1 Incidence

STS is a rare tumour among CYP, accounting for 6% of total childhood cancer, and 4% of TYA cancers [39, 75]. Rhabdomyosarcoma was more common among children aged younger than five with an incidence of 6.5 per million person-years, while it was 3.9 among TYAs [50]. The incidence of non-rhabdomyosarcoma was more common among TYAs with an incidence of 11.9 per million person-years, compared with 4.4 among children (Figure 9) [50].



Sources: http://www.cancerresearchuk.org/health-professional/cancer-statistics/childrens-cancers/incidence#heading-Seven

Figure 9: The average annual incidences of soft tissue sarcoma in million person-years in the UK among children aged 0-14.Data Sources [41]

2.3.12.2 Evolving cancer treatment

Soft tissue sarcomas are more common among adults than children [119, 120]. Young adults had a lower response to treatment compared with children. Among all age groups 90% had chemotherapy, 59% were treated with surgery and some had radiotherapy, while adults with localised tumours were mainly treated with surgery [121]. The use of chemotherapy was found to improve the overall survival rate, however it was suggested

to limit the use of chemotherapy to cases with unresectable tumours [122]. It was recommended that low risk groups be followed-up four to six months after treatment completion for any relapses, and high risk groups followed up every three to four months [121].

2.3.12.3 Survival

Children with STS had the worst survival rate compared with other cancer types, with 73.4% improvement in 2001-2010 [54]. The survival of STS was better among children and older adults than TYAs [43, 90].

2.3.12.4 Cancer related morbidity

Soft tissue sarcoma had 1.23 relative risk of long-term morbidity related to hospitalisation [23]. These patients were at risk of chronic diseases compared with their siblings. They were hospitalised 1.82 relatively more than the background population and had 1.26 longer stay [15]. However, these were admissions among long-term survivors for all types of admissions combined. Hence, there is limited knowledge of the type of morbidity that frequently occurred among STS and the factors that influenced the pattern of admission from the date of diagnosis.

2.3.13 Germ cell tumours

2.3.13.1 Incidence

Germ cell tumours make up the third most common cancer group in teenagers and young adults. It is more common among older children aged above 15 years with an incidence of 30.9 per million person-years, whereas the incidence is less than 7 among children. It is more common among males than females.

2.3.13.2 Evolving cancer treatment

A wide range of trials have been presented for germ cell cases, these have focused on reducing the treatment toxicity, such as reducing doses of chemotherapy, thus improving overall survival rates [123]. However, the decision to reduce treatment needs to be confirmed by experienced oncologists. Further updated results show evidence of improved outcomes for germinoma survivors by reducing the doses of radiotherapy, suggesting prolonged survival period [124].

2.3.13.3 Survival

The survival rate among children younger than 15 years improved from 44% to 91% between 1971/75 and 2001/05 [32]. The five-year survival rate among TYA was 82% which was lower than children (survival rate= 91%), but was better than older adults (74%) [90]. The survival rate among testicular cancer in 2002-2006 was 96.1%, and it

was slightly lower for ovarian cancer, as the survival rate was 79.5% [43]. These were better among TYAs than older adults and were more significant for ovarian cancer.

2.3.13.4 Cancer related morbidity

Three percent of cases relapsed during the first 15 years after diagnosis [125]. In addition, as a result of chemotherapy, germ cell tumours experienced cardiovascular diseases and metabolic syndromes [125]. The rate of hospitalisation after adjusting for the background population was 1.7 for endocrine disease, more precisely, diabetes [87].

2.4 Management of healthcare services

The improvement in survival rates, as noted earlier, was more rapid among children than TYAs. This could be partly explained by the availability of historical epidemiological literature on childhood survivors and the earlier improvement in services by providing a multidisciplinary collaboration of varied healthcare providers, including surgeons, oncologists, radiotherapists and other clinical and non-clinical personnel. This collaboration is responsible for ensuring continuous health provision among childhood survivors, thus improving the quality of health after diagnosis with cancer, compared to 40 years ago [126]. Although the multidisciplinary concept is available among TYA survivors, it is still developing and was formally established during the last 10 years after the release of the National Institute for Health and Care Excellence (NICE) guidelines in 2005 [127].

In 2005, NICE introduced Improving Outcomes Guidance for children and young people with cancer . It includes guidelines based on an evidence-based literature review and cover the following areas:

- Age-appropriate support facilities and staff with appropriate training for this specialised field
- Clinical protocols agreed with principal treatment centres (PTCs)
- Participation in clinical trials

Consequently, PTCs for children and teenagers were introduced as secondary or tertiary centres that provide: tumour-specific centres, a final diagnosis, an agreed upon treatment plan, specialist palliative care and a multidisciplinary team (MDT) for distinctive types of cancer that require intensive treatment (to be discussed in the following sections). Because of the limited number of specialists and low frequencies within multiple diagnostic groups, PTCs could be allocated only at the regional level. Therefore, shared care arrangements were established to provide specialist local patient care to reduce distance barriers, and, as a result, shared care units (SCUs) were assigned to provide supportive inpatient and outpatient care, palliative care and treatment under the

supervision of PTCs for children, and designated hospital for TYA. PTCs have the responsibility for administering types of treatments that are delivered in shared care units.[67].

England had the worst survival rate in comparison with other European countries for all age group [128]. In Northern England, the five-year survival rate for TYAs (15-24) in general increased to 85%, and ALL, AML, NHL and bone tumours had the highest improvement rate during the study period (1968-2008) [55]. Consequently, the NHS set an outcome framework in England for 2013-2014, including essential indicators to reflect the coverage of health services and to ensure the equity and quality of health delivery and outcomes for all, such as: “an indicator of children and young adult people’s experience of healthcare”, “five-year survival of all cancer in children” and “one-year survival for all cancer” [129].

Clinical commissioning groups (CCGs) were give a target to improve the quality of healthcare services by providing a benchmark of current services. These groups were established by the NHS and NICE to be able to prioritise the necessary improvements. One of the main indicators was to set one- and five-year survival rates for all types of cancer in all age groups. The majority of survival studies among paediatric patients assess the one-year and five-year survival rates, while most of the TYA studies use only the five-year survival rate.

The types of services cancer patients need after diagnosis are separated into two periods: the anti-cancer period and the supportive period [130]. Chemotherapy, radiotherapy and surgery are provided during the anti-cancer treatment period, and the supportive period entails palliative care, rehabilitation and follow-up visits, which can be taken during and after treatment. Cancer patients, in particular TYAs, are a very complex group and receive care in different settings, including both specialist and non-specialist SCUs. This raises the question as to whether two patients aged 16 treated in the UK, one in a specialist unit and the other in a non-specialist unit (either paediatric or adult), will exhibit variations in hospital activity rate. To answer this question, we need to be familiar with the healthcare services available for CYP in England, as listed below.

2.4.1 Cancer units, cancer centres and principal treatment centres

A cancer unit is considered to be a district facility that treats common types of cancer. It provides prognostic and basic treatment services, such as chemotherapy, while complex chemotherapy and radiotherapy is provided in a cancer centre. The units are allocated in local areas close patient residences, and are directed by a lead clinician.

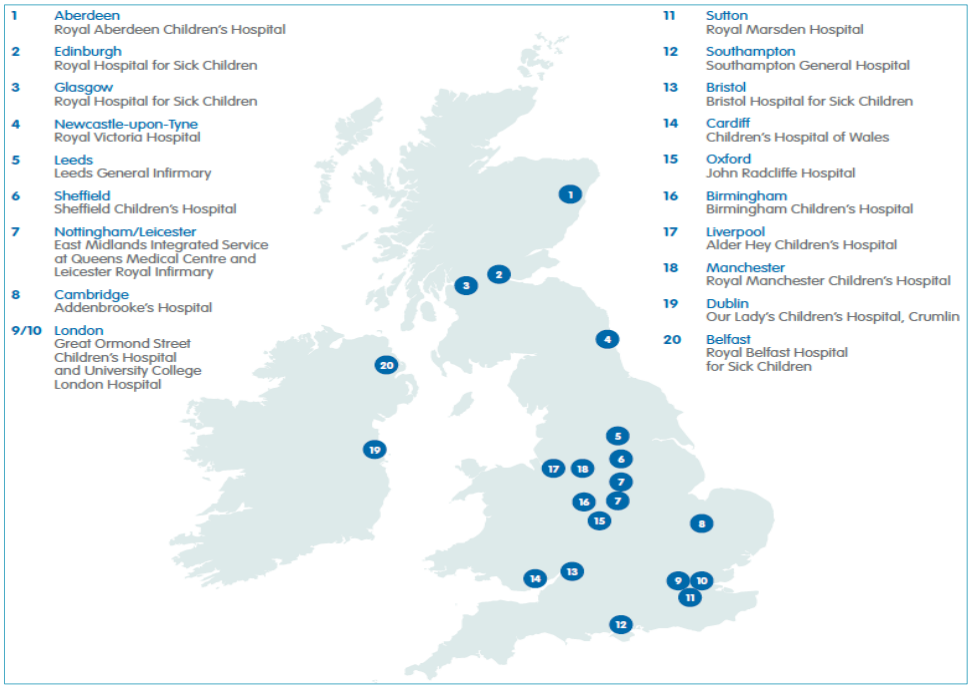
A cancer centre is a tertiary hospital that treats all types of cancer (both common and rare), and is usually placed to cover a wide-ranging area, similar to a regional authority.

In centres, a variety of cancer types are treated with experienced specialists where their experience gained by treating critical mass of cases, and the availability of multi-disciplinary team.

TYAs with cancer were treated in more than one setting, i.e., they could receive treatment in both cancer units and centres [8]. This lack of centralisation in receiving treatment could affect patient outcomes in terms of survival. TYAs are usually treated in specialist units in cancer centres, although not every cancer centre has such a unit. As a result, TYAs can be treated in extra-regional centres [8].

The hierarchy of services is dependent on patient age, as mentioned in the 2005 NICE improved outcome guidelines; patients under 13 are treated in paediatric centres, 14 to 18 year-old patients can chose between being treated in an age-appropriate centre such as a teenage cancer trust (TCT) units [131], that is located in a PTC or paediatric centre, and at the ages of 19 to 24 they have the choice of being treated in the TCT unit or adult centre. Australia, New Zealand and the USA have followed the UK TCT services, which indicate the success of this intervention in cancer specialist services [34, 127]. In 2009, there were some modifications to the guidelines, which encouraged the inclusion of 13 year-old patients in TCTs. Some paediatric hospitals allocate specific wards for TYAs, and some adult settings provide similar services. PTCs, as described earlier, are regional settings that could be far from the residences of TYAs; however, the 2011 review of the IOG allocated more local “designated hospitals”, also known as shared care centres, to overcome transportation barriers facing TYAs and their families.

After the IOG, the implementation of PTCs was established in the UK and Ireland, and currently there are 20 PTCs for children (Figure 10). These centres work as tertiary hospitals and provide diagnoses, treatment and supportive care. There are now 27 TCT units around the UK and six in development (allocated within PTCs). These units have been tailored to meet TYA needs and provide support plus inpatient and outpatient care in friendly environments [131]. There was only a marginal improvement in patient care provided in TCT units in terms of survival [34]. Over the last 30 years, paediatric services have developed to such an extent that currently almost 90% of children in the UK are treated in centralised settings by specialist paediatricians. Consequently, tremendous progress was observed among children as a result of encouraging their participation in clinical trials [132]. In response to the 2005 NICE IOG, recent trials expanded the age limit so that paediatric trials now have an upper age limit of 16 years, while adult trials have a lower limit of 18 years [34].



Sources:http://www.cclg.org.uk/write/MediaUploads/Publications/PDFs/Children_and_Young_People_with_Cancer_-_A_Parent's_Guide.pdf

Figure 10: Distribution of principal treatment centres for children in the UK and Ireland
Data Sources:[13]

2.4.2 Centralised vs. decentralised

Centralised healthcare can be defined as the availability of standardised clinical treatment in terms of clinical trials or specialised clinical centres [133], although alternative definitions according to the availability of specialist staff, or according to the number of patients being treated, also exist [7, 133]. Whereas children with cancer are referred directly to age-appropriate cancer specialist units [134], for TYAs they are more likely to be referred to an oncology specialist, a surgeon or a radiotherapist, rather than a centralised and comprehensive cancer unit [7, 37]. Improvements in survival have been shown for childhood cancer following the introduction of centralised healthcare settings [135]. However, the management of care among TYAs is more complex than children due to the age boundaries. Moreover, the availability of age appropriate TYA centres were only established in the last ten years after the introduction of the NICE guidelines in 2005; they were treated in paediatric or adult centres while the centralised centres have been well established among children aged less than 15 for more than 30 years [11]. In the UK, less than one third of TYAs with cancer were referred to a specialist unit, while the majority of children were referred to specialist centres [134, 135]. Similarly, in the US, more than 90% of children were referred to specialist centres, compared with 24% of TYAs with cancer [37]. These variations suggest a lack of standardised

healthcare among TYAs with cancer, thus is inconsistent in managing cancer care among this age group, nationally and internationally.

2.4.3 Specialist centres and multidisciplinary teams (MDTs)

The definition of a specialist centre differs between childhood and adult settings. In paediatric settings, it is simply an age-appropriate centre regardless of the child's tumour type, while in adult settings a specialist centre is a site-specific centre in which cancer is treated by cancer specialist consultants and in which surgery is performed by surgeons who have high surgery volumes for the same cancer type. For adults, a MDT approach is seen as provision of specialist services and patients are known to have better outcomes if they are mainly treated by MDTs [8]. TYAs bridge the gap between children and adults, and the definition of a specialist centre for this group is less well defined. The Calman Hine Report argued that patients between 16 and 25 years of age have the right to access a specialist unit [136], and this was addressed in the NICE guidelines, which state that MDTs are essential in any PTC for TYAs to ensure that patients are referred to high volume centres that are appropriate for the patients' age as well as tumour site, and are located as near as possible to patients' residences.

When children are diagnosed with cancer, they are transferred automatically to age-appropriate centres in the Children's Cancer and Leukaemia Group [53], where their cases are discussed at the regional level by specialist MDTs and where their treatment plans are set. When TYAs are diagnosed, they will be transferred to an age and site specific centre or a PTC that has an MDT specialist in TYA cancer to choose the appropriate treatment plan and to allocate the appropriate place for receiving treatment. Despite recommendation for age- and site- specific centres for all TYAs with cancer, only CNS, STS and bone tumour site-specific centres exist in the UK. Whilst TYAs with other diagnoses are treated in PTCs. MDTs for TYAs usually contain paediatric oncologists, haematologists, clinical oncologists, paediatric surgeons, specialist nurses, pharmacists and dieticians directed by cancer specialist consultants, therefore including experts in childhood and adult cancers.

Teenagers and young adults have various healthcare needs that exceed the needs of younger children, including accommodation of their disabilities due to cancer treatment [135]. Additionally, sharing their experiences with peers of a similar age could encourage TYAs to participate in clinical trials and increase compliance with treatment regimes. The attention was raised regarding the importance of providing TYAs with such a cooperative team [135]. Additionally, the relationship between the transition from paediatric to adult care for TYAs (aged above 18) and the quality of care in terms of satisfaction among long-term survivors has previously been studied [137]. In their study, they emphasised that a collaborative work of "shared care" between the aforementioned providers is

necessary to facilitate this essential transition [137]. Therefore, it is essential that the MDT understands the importance of preparing TYAs during treatment and follow-up for survivors to be transferred to other settings depending on their age, i.e. patients diagnosed in late childhood could start their treatment in a paediatric facility and then continue their care in an adult setting.

The effect of patterns of specialist care on survival has previously been measured in detail for patients under 24 years of age. The trend of specialist healthcare services over time was studied for CNS tumours among TYAs aged 16-24 [127]. In their study, an increase in multidisciplinary work between PTCs, paediatricians, adult oncologists and neurosurgeons was noticed was noticed over time. It was noticed that the improvement driven by the IOG was evidenced in the availability of more standardised treatments among CNS tumour patients [127]. This included having a multi-treatment strategy in which there was a combination of chemotherapy, radiotherapy and surgery. Additionally, they found that in the last cohort, the follow-up period was not sufficient; therefore, the impact of the aforementioned collaboration was not necessarily related with improved survival.

The impact of PTCs on other types of diagnostic groups, such as lymphomas, leukaemia and other solid tumours that commonly exist among children and TYAs, have not been studied in depth. The relationship between speciality of care and hospital activity is also missing from the literature. Patients treated in specialist care settings can have a greater advantage in attaining optimal care, although little is known as to whether hospital activity varies directly or indirectly according to speciality of care.

Chapter 3 Hospital Activity Literature Review

3.1 Introduction

As described in Chapter 2, cancer survival rates among CYP have improved substantially over recent decades, from 20% in 1960 to 80% in 2005 [75], and despite the recommendation for all CYP to be treated in high-volume age- and site-specific centres [67], there are inconsistencies across England, especially for TYAs [8].

CYP cancer patients are usually admitted to hospital from the point of diagnosis to receive proper investigations and treatment, and they continue to be admitted after completion of treatment as a result of therapeutic-related conditions. The aim of this literature review was to identify the factors that influence hospitalisation use, such as: age, sex, socioeconomic status and ethnicity, place of care and treatment protocol. Furthermore, to identify whether the place of treatment was associated with the quantity of care patients receive. An additional question relates to whether hospital activity rates vary between long-term and short-term survivors. These aims were addressed through comprehensive analysis of the current knowledge regarding hospital activity delivered to CYP.

The following section starts by providing a description of the search methodology adopted, and the search results. It is followed by a detailed assessment of the published evidence regarding the patterns of hospital activity and the related factors, as well as how it varies among survivors and patients who died during the follow-up period. Finally, there is a discussion of the available evidence, and clear gaps in the knowledge of hospitalisation rates are highlighted.

3.2 Methods

This literature review was based on searches carried out based on Ovid, one of the oldest online medical libraries, and specified three databases: Embase, Medline and Leeds University Library. Additional articles were drawn from the set of identified references or recommended by colleagues. Furthermore, Google Scholar was used as a supportive database to find full text articles. A PICO strategy was adopted, which includes the following elements: Patient or population, Intervention or exposure, Comparison group and Outcome to ensure a comprehensive literature search was completed based around a clearly formulated research question. Based on this strategy,

all of the keywords and medical subject heading terms, which provide synonyms for the search key words used, were tabulated (Table 1).

The aims of the literature review included identifying the pattern of hospital admissions and length of stay delivered to TYAs compared with children, and how this is influenced by place of care. Hence, the 'intervention' occurs where the patient is receiving their care. The conjunction command 'OR' was used to allow for varied synonyms from the same field. For example, all the words that were found under the 'outcome' field were linked with 'OR'. Subsequently, all the words were combined using the 'AND' command to restrict the results to the PICO terms. The results were restricted to papers published after 1st January 1996 and written in English. The quality of the documented hospital episode data was better after 1995 in England. Therefore, it was easier to understand the healthcare services that were delivered since that date. The results of the three databases were exported into Endnote and any duplicate files were removed. Full bibliographic details and paper abstracts were uploaded to be reviewed. Two steps were performed before reading the article in detail. First, the title was checked to determine whether it was relevant. Second, the abstract was read and only relevant papers were included.

Table 1: List of the literature review key words using the PICO strategy

Outcome	**Study population (population and comparison group)**			**Intervention**
Activity*	Adolescence*	Cancer*	Childhood	Specialist
Admission*	Adolescent*	H#ematology	Children	Specialist centre
Attendance	Adult*	Hematology	Pe#diatric*	Specialist unit*
Burden of morbidity	Teenager*	Malignancy	Pediatric*	Place of care
Health burden	Young people	Malignant		Teenager* trust
Hospital contact	Young adult*	Tum#r*		
Hospital activity*		Tumour*		
Hospital attendance				
Hospital burden				
Hospital contact				
Hospital rate				
Hospital service*				
Hospitali#ation				
Hospitali#ation rate				
Inpatient				
Inpatient activity*				
Length of stay*				
Bed day*				
Bed day* rate				
Resource*				
Service*				
Utili#ation				
Utili#ation of care				
Utili#ation of health care				
Utili#ation of hospital resource*				

Symbols: * = Truncation method used to retrieving all words with the same stem but with variant endings: # = Wildcard method used to retrieve words that had more than one possible spelling (British vs. American)

3.3 Results

After removing duplicate entries, a total of 601 articles were obtained from the three databases; details of the number of articles obtained through the searching process are illustrated in Figure 11. From these, only 217 were studied in detail because they had relevant titles and abstracts. Only 30 articles studied hospital activity and the use of hospital resources among CYP with cancer. Key data were extracted, including the study

period, study population, outcome measures and study strengths and weaknesses (Table 2).

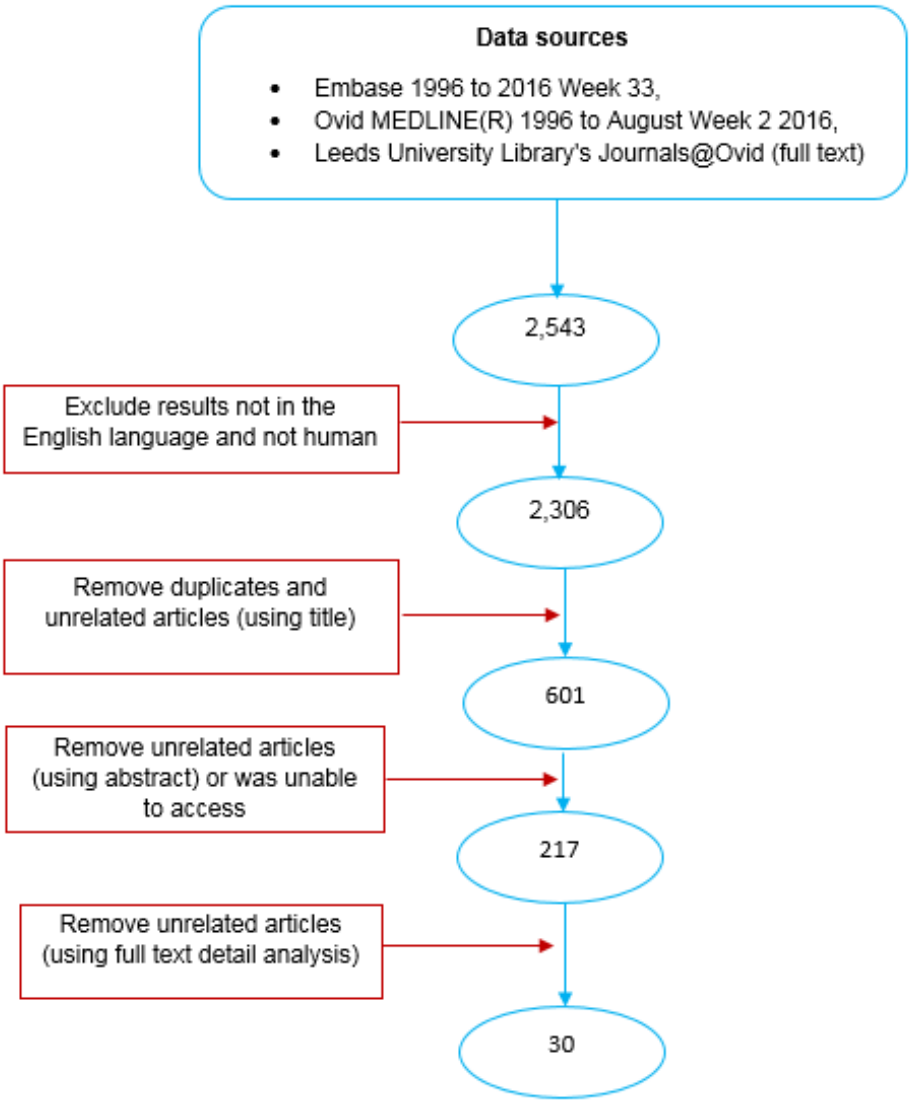


Figure 11: Flowchart of the number of articles identified in the literature review

Table 2: Summary of the systematic review

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Ross, et al. [2003] [138]	Psychiatric hospitalisations among survivors of cancer in childhood or adolescence	Denmark	Diagnosed 1943-1970, admitted 1970-1993, 3,710 individuals	<20	All cancers	Whether they receive radiotherapy or not	Incidence rate of psychiatric admissions among cancer cohort compared with age, sex and period of admissions comparison group.	70% of cases were at risk of psychiatric hospitalisation five years following diagnosis, the relative risk of admissions was 1.3, 95%CI:1.1-1.4).	Used population based registries linked to administrative data.	Contained historical data, hence treatment strategies were changed since then, additionally cases diagnosed from 1943-1967 were lost from follow-up as data was not available back then.
Johnson, et al. [2004] [20]	Hospital attendance patterns in long term survivors of cancer	Yorkshire, UK	2001, 385 individuals	15-44	All cancers	Deprivation, education and employment	Hospital follow-up clinic attendance	Most affluent have higher proportion of attenders, while least affluent have lower proportion of attenders (possibly low compliance in more deprived groups).	Analysed the effect of deprivation and education on survival.	Cross-sectional, limited to long-term survival five years after treatment, attendance limited to hospital follow-up clinics.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Yabroff, et al. [2004] [26]	Burden of illness in cancer survivors: findings from a population-based national sample	US	2000, 1,823 cancer cohort and 5,469 control group	15->70	All cancers	Time since diagnosis	Compare health burden among cancer survivors compared with age, sex and educational attainment matched population. Health burden identified as: utility, morbidity, day lost from work and length of stay.	Cancer survivors had poorer health, lower productivity, spent more time in hospital, lost large amounts of their working hours and experienced more morbidity.	Assessed financial health burden (employment, loss of working hours and physically (diseases).	The analyses were limited to adult survivors, didn't adjust for age at diagnosis and their data were extracted from questioner, hence increased the chance of recall bias.
Rosenman, et al. [2005].[18]	Hospital resource utilisation in childhood cancer	Indiana, US	1995-1997, 165 individuals	<18	CNS, lymphoid, solid tumours, myeloid leukaemia	Gender, age, diagnostic group	Number of hospitalisa-tions, length of stay and cost	Mean 44.5 bed days and 6.6 admissions per patient, each patient had on average stay of 6.7 bed days per admission.	Assessed short term treatment effects	Limited to three-year period after diagnosis, selection bias (only include patients with an available hospital administrative record), not population-based.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
The National Institute for Health and Clinical Excellence [2005] [11]	Guidance on Cancer Services Improving Outcomes in Children and Young People with Cancer: The Manual	England	Not Applicable	0-24	All cancers	Year of admission	Rate of bed days inpatient and day case per 1,000 people by years of admissions and age group	Slight increase in the bed-days by year from 1996-2002.	Provided an overall trend of hospital stays.	Was not clear if it was for cancer patient or for all admissions among CYP.
Hendrickson and Rimar [2009] [79]	Patterns of hospital resource utilisation of children with leukaemia and CNS tumours: a comparison of children who survive and those who died within three years of diagnosis	US	2000-2004 223 individuals	<18	CNS and leukaemia	Cancer type, type of admission, vital sign (alive or died)	Mean admission rates and frequency of admissions	Range of admissions: 0-33 and length of stay: 1-391 days, average of 38.9 bed days per individual. Leukaemia survivors had higher inpatient activity, while CNS survivors had greatest use of ICU.	Compared admissions between survivors and deceased individuals. Information about admission were collected using administrative data.	Did not include teenagers and young adults. Cross-sectional analysis of data at single point in time, used data from only one hospital setting. Simple analysis, no regression models.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Pockett, et al. [2010] [139]	The hospital burden of disease associated with bone metastases- and skeletal-related events in patients with breast cancer, lung cancer, or prostate cancer in Spain	Spain	Diagnosed in 2003, Followed up till 2006, 28,162 individuals	Mean age 60	Breast cancer, lung cancer and prostate cancer	Age and treatment	Mean readmission, length of stay and cost	Cancer cohort with metastases of cancer had higher mean number of re-admission and stay for longer period than cancer cases with no metastases (mean length of stay= 8 vs 18 for breast cancer, 15 vs 22 for lung cancer and 12 vs 19 for prostate cancer).	Described the impact of metastasis of cancer on number of admission and length of stay.	The hospital burdens were not adjusted by age at diagnosis, or the follow-up years or the place of diagnosis. In addition it was limited to adult cancer.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Bradley, et al. [2010].[140]	Hospitalisations 1998-2000 in a British Columbia population-based cohort of young cancer survivors: report of the Childhood/ Adolescent/ Young Adult Cancer Survivors Research Program	Canada	1998-2000 1,816 individuals	<20	All cancers	Relapse, treatment type (radiation, chemotherapy and surgery), rural urban resident, region of residence and deprivation status (area-based index using average income per person)	Hospital admission: taken from discharge report. Odds ratio and relative rate of admissions comparing hospitalised survivors vs. non-hospitalised survivors, and survivors with comparison population.	Odds ratio of hospitalisation among cancer survivors higher than population (2.2 vs. 1.5), length of stay higher among cancer survivors (relative risk (RR) is 1.71), survivors also had more day care visits RR 2.99.	Took into account socio-economic status and clinical difference when comparing hospital admissions among five year survivors. Compared the pattern of hospitalisation between relapse cases and non-relapsed cases.	Possible selection bias since only the completed record was analysed; if patients had two admissions on the same day they took the longest stay hence could overestimate the length of stay. When calculating admission rates, did not take into account place of care.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Lorenzi, et al. [2011] [141]	Hospital - related morbidity among childhood cancer survivors in British Columbia, Canada: Report of the childhood, adolescent, young adult cancer survivors CAYACS program	British Columbia Canada	1986-2000, 1,374 survivors and 13,740 control group	0-20	All cancers	Gender, age, year of diagnosis, time since diagnosis, treatment modality, and relapse status	Frequency of admission among cancer survivors compared with control group, and relative risk of morbidity	The risk of morbidity decreased by follow-up years; survivors of bone tumours had higher morbidity risk compared with leukaemia survivors. Cancer survivors had higher risk of morbidity compared with control group for all causes especially for neoplasms and disease of the blood.	Analysed the factors that affect hospital related morbidity, and identified the relative risk of admissions compared with control group.	Limited childhood to long term survivors, did not assess the impact of deprivation, ethnicity and place of care on hospitalisation use in term of admissions only, i.e. did not assess burden of length of stay.
Maddams, et al. [2011] [142]	A person-time analysis of hospital activity among cancer survivors in England. British Journal of Cancer	England	1990-2006	All ages group	Colorectal, lung, prostate and breast cancer	Age, gender and year since diagnosis	Rate of hospital stay among survivors by years since diagnosis and age	Number of days per person - days decreased by years since diagnosis.	Using person time at risk in assessing the difference of length of stay by age and time since diagnosis.	Did not adjust for treatment duration and limited to cancers among older adult.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Maddams, et al. [2011] [143]	Levels of acute health service use among cancer survivors in the United Kingdom. European Journal of Cancer	England	1990-2006, 1,625,340 survivors	All ages group	Colorectal, lung, prostate and breast cancer	Age, gender, cancer type, years from diagnosis and years to death	Percentage of survivors with hospitalisation in term of time spent in hospital by years since diagnosis and years to death.	Cancer survivors had the highest level of hospitalisation during one-year following diagnosis and before death.	Assessed difference in proportion of hospitalisation by gender from date of diagnosis.	The calculation of proportion of hospitalisation was based on grouping cases into categorical groups based on: temporal admission and level of utilisation rather than using continuous measure.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Tuppin, et al. [2011].[13]	Hospitalisation admission rates for low-income subjects with full health insurance coverage in France	France	2007 40,155 million insured by national income and 4,791 million covered by complementary universal health insurance for low income people	<60	Any disease requiring hospitalisation (including cancer)	Age, sex hospital department of admission	National health insurance reimbursement to calculate type and rate of admission	1.4 hospitalisations per patient, the mean length of stay was 3.1 days. Highest hospitalisation activity seen for females due to radiotherapy and chemotherapy	Assessed hospitalisation patterns taking into account gender and treatment differences.	Measured all types of admissions, not only cancer. Did not take into account if the admission was before or after diagnosis, nor whether patients died.
Kurt, et al. [2012].[12]	Hospitalisation rates among survivors of childhood cancer in the Childhood Cancer Survivor Study cohort	US	1994-1996 (baseline) and an updated questionnaire in 2000-2005, 10,366 individuals	0-20	Leukaemia, lymphoma (HL, NHL), CNS, bone, Wilms' tumour neuroblastoma, STS	Age, sex, cancer type, and detail treatment type	Standardised incidence ratio among cancer survivors compared with general population	1.6 times higher rate of hospitalisation than the background population	Examined multiple factors that could affect hospitalisation among cancer survivors, using large cohort population.	Questionnaire based so might have information bias (recall bias), period of diagnosis and length of survival was not recorded.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Audino, et al. [2013].[144]	Length of stay and treatment - related complications are similar in paediatric and AYA patients with bone sarcoma in United States children's hospitals	US	2006-2010 835 children and 562 TYAs	0-14, and 15-28	Bone sarcoma	Age, sex, source of payment and hospital charge	Mean length of stay(LOS)	Mean LOS = 4.6 (children)and 4.8 (TYA)	Compared frequency of length of stay among children and TYAs, and identify the difference of cases of admissions.	Hospital admission coverage limited to 25% of total paediatric population. Date/age at diagnosis and survival time were not recorded. Not clear if the admission was for recurrent cancer or primary cancer.
Berger, et al. [2013].[19]	The burden of cancer on the acute medical unit	North west of England	2011 300 individuals	16-98	All cancer combined	Age and sex	ICU unit hospitalisation (length of stay). Comparing cancer patients with other patients without cancer matching on age and sex.	Cancer patients had significantly longer stay in hospital (8.8 vs. 7.2 days on average-mean).	Focused specifically on hospital activity within ICU.	Cross-sectional and do not adjust for follow-up period, date of diagnosis and period of survival was not recorded.

Birch [2013] [8]	Teenage and young adult cancer in England – the patient journey and experience	England	2001-2006 9,026 individuals	15-24	All types of cancer as specified in Birch (2002) scheme	Cancer type and, place of care	The impact of specialist services on survival outcome	The coverage of specialist care varied by cancer type among TYA. There was significant variation in the relationship between levels of TYA specialist care and survival rate by cancer type. For some cancer types such as leukaemia, CNS tumours and lymphoma patients receiving higher levels of specialist care exhibited better survival rates. For most cancers, those with a higher proportion of specialist care had longer hospital stays than those with lower level of specialist care.	HES data (national database) was linked to several cancer registers that cover the majority of England.	Did not provide the pattern of hospitalisation for children. Did not adjusted for treatment duration when estimating the number of admissions and length of stay.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Brewster, et al. [2014] [101]	Subsequent hospitalisation experience of five-year survivors of childhood, adolescent, and young adult cancer in Scotland: a population-based, retrospective cohort study	Scotland	1981-2003 6,980 individuals	0-24	All cancers	Age, sex, deprivation (area-based Carstairs), follow-up period, diagnostic group	Indirect standardised incidence ratio for calculation of bed days, acute hospital admission and psychiatric admission, absolute excess risk of bed days and admission, cause specific admission (ICD-10)	Indirect standardised bed days ratio=3.7 per 100 survival compared with population. Standardised rate of hospital admissions =2.8 per 100 survival. CNS have the highest admission for acute care where most of these admissions are related to recurrent neoplasm, nervous system diseases. Hospital admission was higher among most deprived survivors.	Population-based study with long follow-up period, full details of the classification used for cancer and admission related causes.	Limited to long term survivors (five years+), did not take into account period of diagnosis, treatment type or place of care.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
de Fine Licht, et al. [2014] [72]	Hospital contacts for endocrine disorders in Adult Life after Childhood Cancer in Scandinavia (ALiCCS): a population-based cohort study	Scandinav-ia	1943-2008, 43,909 cancer registry	0-20	All cancers	Gender, age and cancer type	Standardised hospitalisation rate (SHR) and absolute hospitalisation rate among cancer survivors compared with control group	SHR= 4.8, highest risk was for leukaemia (SHR=7.3) followed by CNS tumours (SHR=6.6), the absolute risk of admission for endocrine disorders was 1,000 per 100,000 person-years.	Detailed analysis of hospital admission for endocrine disease sub types among short term survivors (within one year after diagnosis).	Limited to one type of morbidity and did not adjust for treatment type.
Hargreaves and Viner [2014] [145]	Adolescent inpatient activity 1990-2010: analysis of English Hospital Episode Statics data	England	1999-2010, 9,632,844 hospital episodes	0-19	Not cancer specific data	Age, year of admission and causes of admission based on ICD-10 chapter	Number of admission per thousand person-years, trend of percentage of admission by year	Number of admissions increased by age and it was higher among males in children and females in adolescents.	Described the pattern of admission by age and year of admission.	Was general for all cases regardless of the disease background.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Holmqvist, et al. [2014] [87]	Adult life after childhood cancer in Scandinavia: diabetes mellitus following treatment for cancer in childhood	Scandinav-ia	1940s-2008, 496 survivors	0-20	All cancers	Cancer types, time since diagnosis	Standardised incidence rate of admissions among cancer cohort compared with background population.	Cancer survivors had 1.6 higher rate of admissions than comparison group, and it was highest during the first five years following diagnosis.	Assessed hospitalisation rate for long term, including 50-year follow-up period.	Focused on one type of cause, specific hospitalisation-did not assess the impact of type of treatment on admission rate.
Mahar, et al. [2014] [22]	Predictors of hospital stay and home care services use: A population-based, retrospective cohort study in stage IV gastric cancer	Ontario, Canada	2005-2008, 1,433 individuals	18-99	Gastric cancer	Age, sex, deprivation, region, treatment (surgery) place of care (high volume specialist consultant, receipt of home care)	Comparing relative rate of hospital stays among cases that received specialist care or home care compared with cases who had not.	Patients who received care in high volume oncology had lower hospital stays than cases who did not. Additionally, cancer survivors were at increased risk of hospitalisation one month before death.	Identified the impact of place of care on hospital stay among cases with terminal cancer and provided evidence of possible increase in hospitalisation before dying.	Limited to adult survivors, focused on admissions occurring among cases with aggressive cancer (late stage).

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Stammers, et al. [2014] [68]	Cancer incidence, morbidity, and survival in Canadian first nation children: A Manitoba population‐based study from the cancer in young people in Canada (CYP‐C) registry	Manitoba, Canada	2001-2008, 240 individuals	0-15	All cancers	Ethnicity and risk group (cases were assigned to three groups by oncologist giving: year of diagnosis, stage of the disease, type of surgeries and the availability of treatment).	Standardised incidence rate of hospitalisation among cases from first nation (North American Indian) compared with non-first nation.	There were no differences in number of admissions and length of stay between first nation and non-first nation cases. First nation cases with high risk group had higher number of admissions 7.6 compared with 2.2 per 1,000 days on treatment among cases with lower risk and longer stay (105.0 vs 18.0 per 1,000 days).	Assessed the pattern of admissions and length of stay during the treatment period, and assessed the impact of race on hospitalisation pattern.	Limited to children and included small number of cases, it was difficult to draw a conclusion of the impact of treatment type received, and year of diagnosis on the hospitalisation rate as it was hidden under the arbitrary method used in classifying groups based on level of risk.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
van Laar, et al. [2014].[71]	Cardiovascular sequelae in long-term survivors of young peoples' cancer: a linked cohort study	Yorkshire	1991-2006 3,306 individuals	0-14 and 15-29	All cancers	Age, sex, year of diagnosis, diagnostic group, deprivation (index of multiple deprivation) and initial treatment type	Age and sex standardised incidence of cardiovascular disease for cancer cohort compared with population	3.6% of survivors had at least one admission for cardiovascular disease during 10 years from diagnosis (IQR 7-13 years), hospitalisation rate for cardiovascular diseases was 2.6 compared with population.	Linked HES and a population based cancer register.	Focused on one type of hospital admission for specific long-term survivors. The place of care was not assessed in relation to the type and rate of admission.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Zhang, et al. [2014] [23]	Late morbidity leading to hospitalisation among five-year survivors of young adult cancer: A report of the childhood, adolescent and young adult cancer survivors research program. International Journal of Cancer	British Colombia	1981-1999, 902 survivors and 9,020 comparison group	20-24	All cancers	Age, gender, region of residence, deprivation, cancer type, year of diagnosis and type of treatment	Prevalence of admissions and relative rate of admissions compared with background population	Cancer survivors were at 1.37 greater risk of hospitalisation than comparison group, and cancer treated with combination of chemotherapy, radiotherapy and surgery at higher risk of admission than cases with chemotherapy alone.	Assessed factors that influence hospitalisation among cancer survivors.	Limited to TYA and long-term survivors, and did not assess for place of care.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Chan, et al. [2015] [146]	A population based perspective on children and youth with brain tumours	Ontario, Canada	2003-2010, 745 individuals	0-19	All cancers	Age, gender and year of admission	Rate of hospital admission per person year using population estimate	Cases with malignant brain tumours had highest hospital admissions than benign tumours. The rate of admissions was slightly increased by year of admission.	Assessed hospitalisation rate by different cancer grades: benign and malignant brain tumours.	Did not assess the follow-up year, date of diagnosis or date of treatment completion.
Phillips, et al. [2015] [147]	Survivors of childhood cancer in the United States: prevalence and burden of morbidity	USA	1975-2011, 388,501 survivors	0-19	All cancers	Age, gender, age at admission, year since diagnosis and ethnicity	Prevalence of admissions by years since diagnosis	There is an increase in long-term childhood survivors; morbidity increases by age	Detailed description of pattern of admission by follow-up years, by gender, and specific morbidity.	Did not assess for deprivation and type of treatment received.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Rahman, et al. [2015] [148]	Incidence, risk factors, and reasons for hospitalization among glioblastoma patients receiving chemo-radiation	USA	2006-2010, 196 individuals	23-90	Glioblastoma	Age, marital status, type of radiotherapy	Frequency of admission, length of stay and mortality	43% of cases admitted during the treatment phase, and these were related to weaknesses and seizures.	Assessed the rate of admission before, during and after receiving the treatment.	Limited to specific cancer type with specific type of treatment.
Richardson, et al. [2015] [149]	Hospitalisation rates among survivors of young adult malignancies	Ontario, Canada	1992-1999, 20,275 survivors and 195,847 comparison group	20-44	All cancers	Age, sex and cancer types	Hospitalisation rate per person year for survivors and comparison group, relative rate of admissions, adjusted relative rate (ARR) and absolute excess risk of hospitalisation.	ARR was 1.51 among cancer survivors compared with control group, upper GI had the highest hospitalisation rate followed by leukaemia. Rate of hospitalisation decreased by follow-up time.	Assessed the hospitalisation rate by detailed cancer type, cause of admission and rate of admission by follow-up period.	Limited to long term survivors, did not assess the effect of ethnicity, deprivation and treatment type on hospitalisation rate.

Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Bhuller, et al. [2016] [70]	Late mortality, secondary malignancy and hospitalisation in teenage and young adult survivors of Hodgkin lymphoma: report of the Childhood/ Adolescent/ Young Adult Cancer Survivors Research Program and the BC Cancer Agency Centre for Lymphoid Cancer.	British Columbia	1970-1999, 281 survivors, 2,810 comparison group	15-24	Hodgkin lymphoma	Gender, age, region of residency, deprivation, year of diagnosis, treatment type and relapse status	Incidence of hospitalisation and rate ratio of hospitalisation	Cancer survivors were 1.45 at higher rate of admissions than comparison group, the admissions were affected by year of diagnosis: cases diagnosed at the latest period have higher rate of admission, and cases treated with combination of modality had the higher rate ratio of admission compared with comparison group.	Assessed hospitalisation rate, adjusted for varied demographic and clinical data, found morbidity specific admissions for TYA surviving from Hodgkin lymphoma.	Limited to long term survivors, did not assess for the impact of follow-up period or place of care or include historical treatment data.

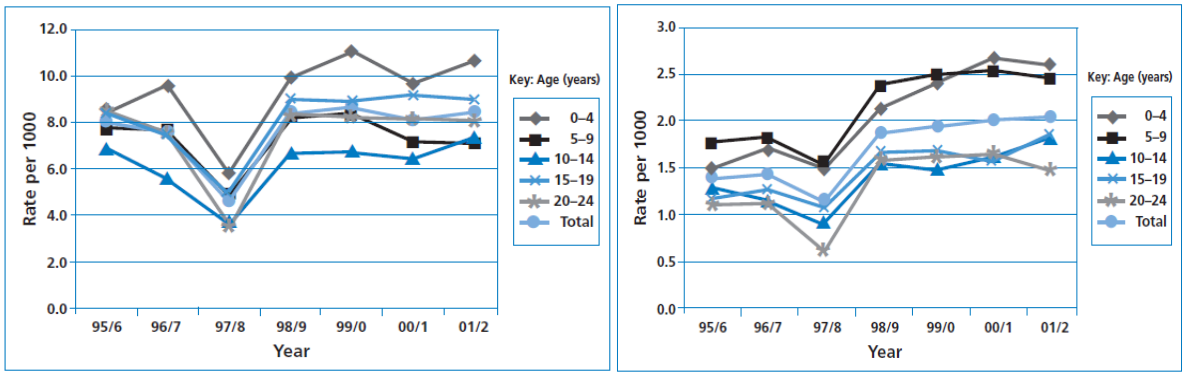
Author, (Year)	Title	Study region	Study period and population size	Age	Diagnostic group	Study variables	Outcome measure	Key findings	Strengths	Weaknesses
Sieswerda, et al. [2016] [150]	High hospitalisation rates in survivors of childhood cancer: A longitudinal follow-up study using medical record linkage	Amster-dam	1996-1999 1,382 survivors and 26,583 comparison group	0-18	All cancers	Gender, cancer type and treatment	Hospitalisation rate among cancer survivors and control group, relative hospitalisation rate comparing cancer cohort with control group	Cancer survivors are at continuous risk of admissions 30 years following diagnosis with relative risk of 2.2. Relative rate of admission was higher among CNS survivors than other cancer types.	Assessed hospitalisation rate among cancer survivors compared with control group using 30 follow-up years.	Limited to long term childhood survivors aged above 18, and did not adjust for deprivation, ethnicity or place of care.

3.3.1 Hospital activity

Analysis of hospital utilisation provides an understanding of health burden and morbidity thus facilitating the planning of services. However, no published study to date has analysed the pattern of hospital admissions of survivors both during and after completion of cancer treatment among CYP. With emerging evidence of patients experiencing a better quality of life in terms of their survival rates if treated (at least in part) in specialist centres for some cancer types such as leukaemia, CNS tumours and lymphoma [8], analysis of the different patterns of hospital usage among patients receiving mostly specialist services, compared with those receiving only limited or no specialist services, could provide policy makers with the evidence required to plan services needed for CYP survivors to receive optimum care. Such work will also identify those groups of cancer patients who exhibit the greatest burden on hospital services through side effects and late effects of therapy, therefore allowing healthcare planners to develop changes to care pathways to minimise hospital activity.

3.3.2 Patterns of hospital activity

From 1998 to 2000, there were 3.7 hospital episodes per 1,000 CYP under the age of 24 in the UK [11]. As shown in Figure 12,there was a sharp drop in the usage of hospital beds in 1997/8 after an increase from 1995/6 to 1996/7, however usage began to increase in 1998/9 and continued increasing thereafter. The drop in usage was as a result of poor documentation during that time [11]. TYAs were the second highest patient group using inpatient hospital beds (Figure 12), just after children under the age of five (around 9 and 11 uses per 1,000 population, respectively). Patients under the age of five and TYAs aged 15-24 years had higher incidence rates compared with children aged 5-14, which was reflected in their high usage of hospital beds [11]. Nevertheless, it is not clear whether these visits were for cancer patients or all patients in general. It is also not clear whether the visits were counted after the date of the diagnosis or the completion of treatment. The pattern of day-case services was related to patient age. The average day case bed days ranged from 12,800 for patients under the age 14 to 5500 for patient aged 15-19 and 4,800 for patients aged 20-24 (Figure 12).The causes for these admissions were not recorded, as there was a dearth of available information regarding the relationship between hospital admissions and cancer among TYAs. Procedures, palliative care and allied health services were provided when needed; thus, such data was not routinely collected [11].



(a) **(b)**

Sources:https://www.nice.org.uk/guidance/csg7/resources/improving-outcomes-in-children-and-young-people-with-cancer-update-773378893

Figure 12:Trends in hospital episodes: inpatient bed days (a) and day case bed days (b) from 1995/1996-2001/2002 for children and young people in the UK. Data Sources [13]

Cancer accounted for 3.5% of the total admissions among paediatric cases, and 5% of the total cancer admissions were for paediatric patients, which accounted for 100,000 hospital admissions in the USA [79]. In their study they also stated that CNS cancer and leukaemia patients had a total of 8,653 bed days (38.8 bed days on average per child) and 39.7 hospital admissions on average per child [79]. Children had a higher risk of hospital admissions compared with adults, and needed more intensive care in comparison with elderly patients, which drains a large amount of hospital resources [12]. There was limited knowledge about the scope of hospital activity delivered to CYP in the UK. In the US, however, the use of hospital resources among leukaemia and CNS cancer patients under the age of 18 have been studied previously [79]. However, they only assessed hospital patterns after diagnosis, not after completion of treatment; for example, leukaemia patients treated with chemotherapy required at least three months to recover and for their blood counts to return to normal. Additionally, in their study, leukaemia cases had significantly higher outpatient admissions compared with CNS cancers, while the latter group had a higher number of inpatient admissions [79]. These differences could be indicative of the type of treatment administered. Leukaemia patients usually receive chemotherapy on an outpatient basis. In contrast, CNS cancer patients usually require surgery and radiotherapy, which needs to be provided in a hospital setting. As a result, the type of treatment could affect the pattern of hospital activity. Few studies analysed the admission rate during the treatment period, but a study conducted in USA found that 43% of cancer cases were admitted to hospital due to treatment side effect such as weakness or a seizure [148]. Identifying these complications could help in planning for services to improve quality of life and reduce hospital utilisation.

CYP who survived five to ten years after diagnosis had a high risk of hospitalisation, particularly among leukaemia, CNS and bone tumour diagnostic groups. The age-sex

standardised hospital admission rate ratios for cancer were, 4.5, 3.9 and 3.8, respectively, for each diagnostic group [101]. This was also supported by a population-based study in Yorkshire, UK [71]. In those studies they did not take into account relapses following the primary diagnosis, and they did not study the differences in hospital activity between the primary diagnosis and the activity after the recurrence of cancer [101]. It is essential to understand when the patient has been admitted to be able to understand the cause of the admission. In particular, was it as a result of treating the primary diagnosis or was it as a result of treating the recurrence of cancer following the primary diagnosis?

It was observed in previse studies that 3.6% of the total CYP (aged 0-29) long-term survivors in Yorkshire experienced at least one admission related to cardiovascular disease [71]. Leukaemia and bone tumours had the highest cardiomyopathy admissions, while patient with CNS tumours had the highest admissions for nervous system and cerebrovascular diseases [71]. The variations in the pattern of admission could be related to the type of treatment delivered by each cancer type, e.g., chemotherapy, radiotherapy, stem cell transplant or surgery. Thus, the type of treatment provided for these patients was analysed in relation to admission rates in the Scotland study [101], and found both the type of treatment and cancer type to influence the pattern of hospital admission, i.e. patients with the same cancer type did not necessarily have similar proportions of admissions if they were treated differently.

Cancer survivors, in addition to the frequent hospital admissions, spent more time in hospital compared with individuals that had not experienced cancer in their life,14% of individuals who had cancer stayed longer than 10 days in hospital, compared with 8% of individuals with no cancer [26].

3.3.3 Patterns of hospital activity after completion of treatment

In some studies it was found that one-half of the admissions occurred 4.5 months after diagnosis [18], while others found that admissions for autoimmune diseases were highest during the first five years following date of diagnosis [74]. However, in their study, they did not adjust for treatment type; hence, the potential cause of admission could be related to the type of treatment received. Patients receiving chemotherapy might be at a greater risk of hospital admission due to infections, while patients receiving radiotherapy could have a higher risk of ICU care. Therefore, it was necessary to take into account the variation in treatment plans (period of treatment, and type of anti-cancer protocol) when studying the variation in hospital activity across diagnostic groups. Within the limited range of literature, the analysis of hospitalisation rate was based on the five-year since diagnosis measure as a proxy for treatment completion, and they found an increase in the proportion of hospitalisation use among long-term survivors [23, 70, 72, 141, 149, 150]. The highest proportion of admissions was among survivors of more than

five years, compared with cases who survived for fewer than five years after diagnosis as found in previous studies [147]. However, they did not assess the pattern of admission and related factors among those survivors from the date of diagnosis.

Completion of treatment can vary depending on treatment type. Patients receiving chemotherapy may need up to three months recovery period after completion of treatment, while stem cell transplant patients may need up to 12 months of recovery (more detail in Chapter 4). Understanding the relationship between treatment type and duration of recovery will help to differentiate the type of admission and whether it is related to a treatment plan or a treatment complication.

3.3.4 Key predictors of hospital activity

3.3.4.1 Place of care

The management of care has evolved during the last decade. Currently, childhood ALL patients receive most of their treatment at home [81]. This change in treatment administration and length of treatment may affect the pattern of hospital care in terms of hospital admissions and prolonged lengths of stays, i.e. it could reduce or increase the use of hospital inpatient bed days and treatment-related morbidity.

Using a national population-based register, The effect of specialist cancer services on TYA outcomes (patients aged 15-24) has been previously studied [8]. In their study, they used a proportional measure to classify the place of care based on their inpatient stay during treatment, rather than a dichotomous measure such as specialist vs non-specialist. This was done due to the fact that survivors could receive their care in more than one setting: including both specialist and non-specialist centres. While there were no differences in the number of admissions between survivors with mostly specialist and limited specialist services during treatment, survivors with some specialist care (defined as having 30-60% of their inpatient stays in specialist centres), tended to have a higher proportion of admissions than other levels of specialist care [8]. They also found that there was an increase in inpatient admissions in teenage cancer trusts (TCTs) which are usually affiliated to specialist centres, compared with non-specialist centres in Yorkshire and North Trent regions [8]. Nevertheless, this might indicate that the availability of specialist care centres could impact on hospital usage. Leukaemia and lymphoma had the lowest median number of admissions when they had limited specialist input during treatment, compared with patients who received mostly or some specialist care. Specialist cancer services provided for individuals with bone tumours and CNS cancers in the UK could be classified into age-related centres (TCTs) and tumour-specific centres. Bone tumours had the highest admissions if treated within TCTs and the lowest admissions if treated in tumour-specific centres, while CNS tumours had the highest

admissions if treated in tumour-specific centres. Despite the inverse relationship between hospital admissions and tumour-specific or age-specific centres, they both displayed the highest frequency of admissions if they received mostly specialist care compared with survivors with limited specialist input. This could highlight the fact that survivors who received the majority of their care during the treatment period in specialist units were more likely to be closely monitored in a multidisciplinary hospital setting. The relation between the survival rates and the level of specialist care was assessed in earlier studies [8]. It was found that the pattern varied by cancer type: leukaemia, lymphoma and bone tumours had better survival rates when treated mostly in specialist centres, while for CNS, STS and germ cell tumours there were poorer survival rates when they received mostly specialist care [8]. However, this study focused entirely on TYA cancer survivors, and did not adjust for person-years of follow-up when analysing the pattern of hospitalisation. Additionally, the impact from the level of specialist care was assessed during the treatment period only, which was arbitrarily defined as 20 months following the date of diagnosis for all cancer types. Some studies used hospitals with high-volume oncology to identify specialist centres; a study that focused on cases with aggressive gastric cancer found a significant reduction in hospital stays when cases received care from a high-volume centre [22]. Cases with terminal cancer contributed to high hospital costs as they were more likely to receive aggressive treatment prior their death, and that increased hospital stays, thus increasing the use of hospital resources [151, 152]. However, receiving care from a specialist centre helped in reducing the unfavourable health burden by properly managing treatment and referring cases to proper home care services, which reduces the use of hospital resources [153]. This highlights the favourable impact of place of care on hospital usage, in term of hospital admissions and hospital stay, however, there is limited knowledge on the impact of place of care on hospital usage among children and TYA specific cancers with varied cancer stage.

3.3.4.2 Gender

Patterns of hospital activity could vary according to patient demographic characteristics and the type of hospital care delivered. The number of admissions could vary by gender boys with ALL historically had higher rates of admissions than girls when younger than 10, however the rate is in the opposite direction during the adolescent period of ages 10-19, where girls had higher rates of admissions [145]. This could be explained by the biological differences, as girls in the adolescent period might be more likely to visit hospitals for obstetric reasons. Similarly, when analysing long-term survivor data, females had higher hospital admissions than males [12]. This was supported by another long-term survivor study, where it was found that there were significantly more admissions among females compared with males, females having 1.56 times higher

rates of admissions than males [23, 140]. When comparing admissions among survivors with a control population, female cancer survivors had higher day case activity encounters and lower acute care admissions than the general population, while male cancer survivors had both higher acute care and hospital day case admissions than the control population [140]. The relationship between gender and hospital activity could therefore vary by type of admission.

3.3.4.3 Age at diagnosis

Hospital admission could also vary according to patient age; young children may need more intensive care than older children due to their sensitivity to treatment [12], for example, children were at more risk of cardiomyopathy due to exposure to anthracycline agents and were at more risk of intellectual disability and endocrine disease when treated with radiotherapy [14, 33, 154]. Furthermore, patients younger than 18 years were found to be more compliant with follow-up visits than those over the age of 18 years. This indicates that younger patients might be more compliant with healthcare treatment, which eventually may lower associated morbidity and subsequent hospital attendance after treatment completion. In previous studies it was found excess hospitalisation among cases aged 25-29 years compared with older adults, suggesting an increase in hospitalisation use according to age [23]. On the other hand, based on data extracted from the Hospital Episodes Statistics (HES) in England, the pattern of admissions was higher among teenagers than children, this was explained by the fact that the mortality rate among teenagers in high-income countries is higher than children [145]. In their study, they explained the overall pattern of admissions regardless of the disease background, hence did not mainly focus on cancer cases. However, children aged younger than 19 had higher hospitalisation rates for endocrine disorders compared with the older age group [72], suggesting that hospitalisation patterns were affected not by age only, but by causes of admission.

Hospital-based analysis in the US shows that TYAs (aged 15-28) had similar lengths of stay as younger children (<14 years old). However, there were significant increases in pain, renal failure and pulmonary effusions among TYAs compared with children [144]. The results of that study might be biased because the age at diagnosis and period of survival were not assessed. Additionally, although the calculation of length of stay was derived from hospital records, it was not clear whether it was from the primary diagnosis or a recurrence; hence, the result could be overestimated, i.e., patients could be counted more than once.

3.3.4.4 Socioeconomic status

In the USA, based on questionnaire data, long-term survivors with low incomes had higher admission rates compared with high income cases; the authors suggest that this may be caused by the fact that low income cases were less likely to come to hospital for regular visits within 2 years of their aftercare [12]. Although healthcare access is different in the USA to the freely provided healthcare in the UK, the findings of the aforementioned studies were not related to patient financial status, because patients with a lower income status were more likely to be provided with government-sponsored insurance for hospitalisation, but not for routine visits to preventive clinics [12]. The rate of admission among long-term cancer survivors had been studied in Canada using a population-based register that took into account the place of residency and socioeconomic status (SES) [140]. Using uni-variable analysis, SES was not significantly related to hospital attendance or place of residence among survivors [140]. Thus, they were assumed not to affect the risk of hospitalisation among survivors. However, others found a significant effect of deprivation on the attendance at a follow-up clinic in Yorkshire, UK [20]. The most affluent patients were more likely to attend hospital than less affluent individuals. Therefore, the relationship between SES and hospital activity could vary between countries and should be considered an important risk factor for hospitalisation.

3.3.4.5 Ethnicity

Hospital admissions might be affected by population background, people with minority ethnicities were less likely to visit a specialist physician, while they were more likely to see a general practitioner [155]. These differences were explained by language barriers, poverty, transportation, physician's attitude, or lack of understanding of the services provided to them [155, 156]. However, only one paper assessed the impact of ethnicity on hospital activity among cancer survivors. This study identified American Indian cases and referred to them as First nation and non-First nation cases. The reason for classifying into these groups is that those groups were from lower social classes, living in rural areas; additionally, they represented 13% of those minorities nationwide in the US [68]. However, there were no noticeable differences in terms of admissions or hospital stays as a result of cancer-related complications during the treatment period [68]. However, their results were based on a small sample size, which reduced the ability to identify significant differences and it was limited to children. Although some of the earlier studies included ethnicity in their study variables, when describing the study population they did not study its effect on hospitalisation [12, 26, 79]. The justification of not including ethnicity in studies conducted in England could be explained by incomplete records of ethnicity in the routinely administrative data, such as HES. The incompleteness of recording ethnicity was attributed to the fact that it is based on multiple resources [157]. Clinicians, radiologists, pathologists and others participate in recording patient records

from which the datasets are extracted to the register. Although HES data is obtained from administrative datasets, the validity varies among the hospital trusts responsible for providing the raw information.

3.3.4.6 Relapse

Relapse following the primary diagnosis was found to be the greatest cause of hospitalisation due to cancer, and relapsed patients were generally hospitalised in intensive care units [140]. Those who experienced relapses had almost double the rates of admission compared to survivors who did not relapse [23, 140], highlighting the importance of this variable in any systematic evaluation of hospital activity. Cancer cases with bone metastasis and skeletal-related events experienced longer hospital admissions than survivors with no bone metastasis [139]. However, in their analysis they focused on older cases, hence there is limited knowledge on the impact of recurrent cancer on hospital use and length of stay among CYP.

3.3.4.7 Cancer types

In a study conducted in British Columbia, bone tumour survivors aged younger than 29 years had a higher risk of hospitalisation than leukaemia survivors [141]. However, others demonstrated that CNS cancer patients had more inpatient visits than ALL patients [140]. Similarly, in previous studies it had been found that CNS childhood survivors had the highest hospitalisation rates compared with other cancer types [150]. Additionally, another study found than childhood brain tumour survivors had a higher incidence of psychiatric disorders than other cancer groups, adjusting for the background population [138]. These differences highlight the fact that hospitalisation use varies by cancer type and age group. Among CYP with brain tumours both malignant and benign tumours contributed to the use of hospital admissions, although the rate of admissions among malignant tumours was 14.9 times higher than benign tumours, and cases with benign tumours had longer hospital stays [146]. This highlights the importance of including both types of brain tumours when analysing the hospital burden to provide healthcare initiatives through accurate assessment of hospital needs among cancer survivors.

3.3.4.8 Type of treatment

Treatment type could also play a predominant role in the rate of admission; patients who received radiotherapy had higher admission rates among long-term survivors than patients receiving surgery, however it was not significant [140]. Cancer cases receive different types of treatment depending on the cancer type, prognosis, age at diagnosis, grade/stage and gender, as explained earlier in Section 2.3.4. The combination of chemotherapy, radiotherapy and surgery was found to increase the risk of hospitalisation

compared with surgery alone among long-term child survivors [141]. Long-term survivors of HL are at risk of recurrent cancer and both pulmonary and cardiovascular-related causes of hospitalisation. The author justifies this higher risk of morbidity as being due to the type of curative treatment administered [12]. Survivors of HL had the highest relative rate of admission when treated with a combination of chemotherapy, radiotherapy and surgery, compared with cases with other modalities [70]. It had been found in previous studies that cases treated with radiotherapy had higher rates of hospitalisation than cases treated with surgery alone [140, 150]. Others found no relation between radiotherapy and admissions among long-term survivors [138]. While some found that the risks of hospitalisation among cases treated with chemotherapy, rather than cases treated with surgery [71]. However these differences could be explained by the study outcome, as in some of those studies focused on admissions for specific morbidity [71, 158], While the rest assessed admissions for all morbidity combined [140, 150]. Therefore, the type of treatment could have a varied influence on the hospitalisation rate, in terms of cancer type and type of morbidity.

3.3.4.9 Deceased during follow-up

Individuals with terminal illnesses such as cancer had the highest use of hospital resources, thus exhausted significant levels of hospital budgets [22]. These utilisations were found to be higher among cases who were less likely to survive [22]. However, there is dearth of information on the pattern of hospital admissions prior to death among CYP with cancer. Only three studies analysed hospitalisation use among survivors and cases who did not survive among children [79] and young adults [22, 143]. The utilisation of hospital resources among children under the age of 18 between three-year survivors and those who did not survive beyond two years following diagnosis were compared in previous studies [79]. In their study, they found that leukaemia patients who died within the first three years had a significantly longer length of stay (7.40 days on average) and higher use of the intensive care unit (ICUs). CNS cancer survivors also had a higher use of ICUs. This could be related to the type of treatment, because CNS cancer patients with high grade tumours require major surgical interventions and need to be monitored intensively [79]. CNS tumour cancer and leukaemia survivors had lower lengths of stay compared with patients who died. Consequently, this could increase the financial burden on hospitals. Of particular note, appropriate palliative care delivered to high-risk patients was found to lower the rate of hospital admissions and eventually save patients and their families travelling time to the hospital. A limitation of this study is that it did not take into account other diagnostic groups and used a single administrative database for data extraction, rather than using a population-based database. Although it was one of the first major studies of the utilisation of hospital services among child and adolescent three-

year survivors compared to non-survivors, the author examined only two types of diagnostic groups in one healthcare setting. The hospital utilisation in terms of time spent in hospital, time since diagnosis and time to death had been studied previously [143]. They found that survivors had the highest hospitalisation use one year after diagnosis and one year prior to death, highlighting the critical periods during which patients require access to high levels of NHS services [143]. However, the study did not assess hospitalisation rates for other types of cancer common among CYP. Another study assessed the pattern of hospital utilisation among cases aged 18 and older and found that the length of stay increased one month before death, however this pattern was lower among cases receiving home care [22]. Their analyses were limited to cases with advanced cancer, thus limiting the knowledge on cases with early stages of cancer.

3.4 Strengths and weaknesses of earlier studies

The existing literature highlighted the fact that CYP with cancer are at higher risk of hospitalisation and varied factors could impact the pattern of hospitalisation. However, the outcome measures for assessing hospital activity or hospitalisation varied, either in describing the variation in hospitalisation internally among cancer survivors or externally by comparing with the background population. The measures included incidence ratios [12, 22, 70, 72, 101, 146], odds ratios [20, 140], absolute rate ratios [101], relative rates [149, 150] or other similar summary measures [18, 20, 23, 79, 139, 141, 143-145, 147, 148], hence this makes it difficult to draw clear conclusions on the effects of patient demographics and clinical characteristics on hospital use, as a way to monitor health services. Odds ratios were suitable for case-control studies in which the control group was matched with cases. However, patterns of care could be more ideally analysed using cohort analyses or retrospective cohort analyses by adjusting for explanatory variables using a suitable regression model, such as the Poisson or negative binomial models. The incidence ratio was acceptable because this takes into account patient characteristics (age and sex), although further analysis is needed to determine the effect of other factors, such as place of care, treatment type and length of treatment which none of the cited papers focused upon. Poisson regression could be used more efficiently to reduce bias in estimates by taking into account other variables that could affect the rate of admission. The literature on hospital activity to date has failed to take into account treatment duration among short-term survivors for both children and TYAs.

Hospital-based analyses in the US have shown that TYAs (aged 15-28) had similar lengths of stay as younger children (<14 years old). However, there were significant increases in pain, renal failure and pulmonary effusions among TYAs compared with children [144]. The results of that study might be biased because age at diagnosis and

period of survival were not assessed. Additionally, although the calculation of length of stay was derived from hospital records, it was not clear whether it was from the primary diagnosis or recurrence; hence, the findings could be an over-estimation of time spent in hospital, since patients could be counted more than once.

The relationship between deprivation and hospitalisation was analysed in a small number of studies. However, different indices of deprivation were used including: Carstairs score, patient income, education, employment, and Townsend score, which makes it difficult to compare the results accurately. However, there was some general consistency in that the most deprived populations had higher levels of hospital activity [12, 20, 79]. This could be because patients from lower SES tend to have lower treatment compliance due to treatment complexity, as shown in an earlier study [81].

3.5 Conclusion

Analysis of hospital burden among CYP cancer survivors was found to be a relatively new phenomenon and identified studies mainly focused on long-term survivors. Besides the small number of published studies, these used a wide range of outcome measures, sub-optimal study designs and lacked appropriate statistical analysis and adjustment for key variables.

Several key variables such as age, gender, deprivation, ethnicity, type of treatment received and place of care were found to be directly related with patterns of hospital activity. The literature provided evidence of differences in hospital activity between short-term survivors and patients who died within that period, however this was limited to three studies and these were not based on population-based data. Hospital admissions and patterns of care are crucially important among young people to estimate their health burden and related morbidity. The value of this knowledge will provide policy makers with evidence of the health burden among the increasing pool of survivors, to provide information to healthcare planners about the risks of hospitalisation due to treatment side effects, and to assess whether any reduction in the intensity of treatment in recent years has led to a lower risk of subsequent hospitalisation.

To address this knowledge gap, information on all CYP newly diagnosed with cancer was extracted from a population-based cancer register and linked with HES data to provide a relatively objective estimate (at least compared to questionnaire-based study designs) of hospital admissions and length of stay for each individual. Additionally, a separate analysis was carried out extract patterns of hospital admissions among survivors from those who did not survive.

The thesis focused on eight specific diagnostic groups: leukaemia, lymphoma, CNS tumours, neuroblastoma, renal tumours, bone tumours, STS and germ cell tumours. These were the most common types of cancer diagnosed among the study population, as explained in the background section 2.3.1. Leukaemia and CNS tumours have been shown to have predominantly treatment-related complications due to the continuous changes in protocols. In contrast, survival rates for bone tumours have been stable over recent decades [42, 54], but have received less attention in terms of development and availability of new clinical studies and trials. In a national, population-based study in Finland from 1953 to 2010, there was continued improvement in cancer treatment, particularly for leukaemia, Hodgkin lymphoma and CNS cancers, which resulted in tremendous improvements in cancer survival [54]. However, bone tumours did not share the same level of improvement and this was because of the delay in enhancing cancer treatment [54]. The patterns of hospitalisation among these diagnostic groups could therefore be related to changes in treatment plans over time. These changes could affect patient outcomes in terms of survival [82], as well as long-term morbidity [101]. Thus, their effects on hospital activity and related morbidity have not previously been extensively studied.

Chapter 4 Material and Methods

4.1 Introduction

This chapter includes details of the study data sources and the analytical methods used. Additionally, details of technical elements are provided that were used to process the study variables in preparation for statistical analysis.

This chapter starts by identifying the main outcome of this thesis, going through a detailed description of the study population. An overview of the YSRCCYP (Yorkshire Specialist Register of Cancer in Children and Young People) is given, as this was used to extract cases and was linked to HES. Individual level datasets were necessary to undertake both linkage and analysis, comprising sensitive and identifiable data, therefore details of ethical and regulatory approval, as well as data security arrangements, are highlighted in this chapter. The cancer classification scheme used to group cancer types is then described, followed by details of variables used to classify ethnicity and measure levels of material deprivation. The main variables derived in this study relate to the estimation of treatment duration, and the calculation of follow-up person-years throughout the admission period. These variables are explained and supported with visual examples in Sections 4.11.3 and 4.12.2. Finally, details of the statistical methods used, which were tailored to meet each aim (Section 4.12) are described.

4.2 Study population

The population comprised CYP aged 0–29 living in Yorkshire when diagnosed with cancer between 1996 and 2009. Hospital admissions were extracted from HES data (1997 to 2011). More details on the study sources are provided in Section 4.6. The study period was chosen so as to be able to assess the total health burden from the date of cancer diagnosis in line with the availability of high-quality HES data.

4.3 Study design

This study aimed to provide a comprehensive analysis of hospital patterns and burden among a cancer cohort of CYP in Yorkshire. Therefore, the study was a retrospective

observational study using linked population-based cancer registration and hospital admissions data.

4.4 Study area

Previous work has shown that the Yorkshire region mirrors the sociodemographic profile of England [56, 62, 159]. The former Yorkshire region contained a population of 2 million aged 0-29 during the 2011 census [44], which had increased from the 2001 census when the 0-29 population was about 1.3 million. In the study area, 38% of the population were aged 0-29, which is similar to the proportions for the rest of England [44]. The study area comprised a slightly higher South Asian population than the rest of England; 9% of the total population aged 0-29 were South Asian, compared to 8% for the rest of England, where the largest majority of the south Asian population were resident in West Yorkshire.

4.5 Diagnostic group

The classification of cancer was based on the International Classification of Childhood Cancer (ICCC-3rd edition) [46], which is commonly used to analyse cancer incidence among CYP, given the need to characterise these tumours according to their morphological features [48, 140]. More detail on the cancer classifications used was provided earlier in Chapter 2, Section 2.2.2.

The current study focused on eight main cancer diagnostic groups: leukaemia, lymphoma, CNS tumours, neuroblastoma, renal tumours, bone tumours, STS and germ cell tumours. The inclusion of these types of cancer was based on agreement with clinical collaborators in terms of representing common diagnostic groups seen throughout the CYP age range. In addition, some of those diagnostic groups, such as leukaemia, were treated with aggressive treatment regimes, including for instance bone marrow transplants, hence these individuals may be at an increased risk of morbidity and thus may exhibit unusual hospital usage patterns. Leukaemia accounts for a third of all new cancers diagnosed among children aged up to 15 years [36], for which they usually receive intensive doses of chemotherapy for a longer duration compared with many other cancer types [160] diagnosed in CYP. CNS tumours account for a fifth of all cancers among cases aged under 30 years [56], and are usually associated with treatment incorporating high levels of radiation therapy, resulting in an increased risk of morbidity and mortality [161]. Lymphoma, neuroblastoma, renal tumours, bone tumours, STS and germ cell tumours were also selected based on their clinical importance and sufficient patient numbers, to ensure that robust estimates of disease burden can be reported. Carcinomas were not included in any detailed analyses as they were relatively rare,

contained a heterogeneous group of cancers and were treated using a range of different modalities. Similarly retinoblastoma and hepatic tumours were rare among those aged above 15 years, which limited the ability to study them in any substantial detail.

4.6 Data sources

Datasets were extracted from the YSRCCYP and linked to administrative hospital records to identify the number of hospital admissions and number of bed days after a diagnosis of cancer.

4.6.1 Case data

Information on the diagnosis and treatment of cancer was extracted from a population-based register, YSRCCYP. The register has accrued cases since 1974 on children up to the age of 15 years, and in 1990 extended into the TYA age range (15–29 years) whilst living in the Yorkshire and Humber Strategic Health Authority. Primary notifications of childhood cancer diagnoses in the region were identified from the regional tertiary referral centre in Leeds, where over 90% of children are treated within the region. These are supported through other multiple sources of ascertainment including regional neuropathology services, the Haematology Malignancy Research Network (HMRN) and cross-checks with the National Cancer Registration Service currently held within Public Health England (PHE) and other specialist childhood tumour registers held in Newcastle (ongoing) and Manchester (until 2013). TYA cancers are primarily notified from PHE and supported through case lists recorded at MDT Meetings at the TYA PTC in Leeds, as well as regional neuropathology department and the HMRN. These notifications include details of date of diagnosis morphology and tomography codes (ICD-O-3) derived directly from the histopathology reports. Reports are scanned and copies retained for future reference, should codes evolve over time. Treatment data including: chemotherapy, radiotherapy and surgeries are pulled directly from medical records, either manually or more recently through electronic processes to improve the efficiency of data collection [49]. All registrations are actively followed-up through contact with hospital consultants and GPs, providing details of any subsequent treatment, relapse or death which has occurred since the period shortly after diagnosis [127]. Completeness in terms of case ascertainment is thought to be extremely high given the multiple sources of ascertainment [159, 162], with around 85-90% of all registrations histologically verified [62, 127, 159, 163].

Key demographic, diagnostic and clinical data were extracted on the following variables: date of birth, gender, date of diagnosis, morphology and topography code, type of initial treatment, name of hospital provider when diagnosed and relapse status. It is worth

mentioning that the YSRCCYP has the advantage of covering 0-29 year olds and has more detailed information on type of treatment received and health status during follow-up, including recurrence or metastases of malignancy [164], than the national cancer register.

4.6.2 Hospital activity

Information about hospital activity was extracted from HES, a national electronic database that contains details of all hospital services provided to patients in NHS funded trusts in England, including different datasets: elective, outpatient and accident and emergency (A&E) admissions and all data collected by the Health and Social Care Information Centre, more recently known as NHS digital (https://digital.nhs.uk/). Information on the services provided by each NHS trust has been collated for reimbursement purposes every financial year 1st April until 31st March [165]. The so-called 'payment by results' [166] system was established in 2002-2003 to ensure that all healthcare providers were paid a standard price (see Section 4.11.3). Hospitalisation details include: diagnosis at admission, frequency of admissions and length of stay, hospital address and treating physician. Each patient has a unique identification number (NHS ID), and this is used to facilitate the follow-up care provided per individual inside England's national boundaries. Inpatient admissions are the most established set of records. Patient admissions were recorded since 1989, but the data accuracy (completeness) and validity were only believed to be appropriate for research purposes after 1996 [48], therefore, all admissions since 1997 were included in the analysis. Outpatient admissions data have been recorded since 2002. A description of the information recorded in an outpatient setting is given in Chapter 6, Section 6.3. Emergency (A&E) admissions were documented from 2007, however, these were not included in this study as linked A&E admissions to the YSRCCYP have only recently become available in 2016.

Using inpatient data solely in identifying the health burden among cancer cases, clearly would provide a limited assessment of hospital burden, as many more admissions will have occurred in outpatient or emergency settings. However, inpatient admissions have been considered to be informative resources for monitoring health services usage and have previously been used in long-term survival analyses [12, 49, 71, 143, 145, 167]. Furthermore, outpatient admissions have been analysed in this thesis to provide a perspective of the outpatient health burden, although the poor quality of diagnostic coding within these datasets limited any further analyses.

Hospital activity was recorded at three levels [168]: 1) finished consultant episodes (FCEs), 2) spells, which are defined as sequential hospital encounters with different consultants which referred as hospital admissions, and 3) continuous inpatient spells

(CIPs), which can be defined as a hospital admissions for the same patient receiving care from different consultants and different providers/trusts within two days after discharge. FCE is the standard measurement unit for hospital activity and is considered to provide more accurate estimates of consultant workload and hospital resources [145] (Figure 13). However, in this project, spells were used to calculate the admission rate and the length of stay because they reduced the overlap in admissions for the same person. A single hospital admissions (also referred to as a spells which lasts from admission to discharge) could include multiple episodes that occurred during the same period of admission i.e. had the same admission date and occurred in the same hospital but with a different consultant. Similarly the length of stay was calculated as the total number of days based on each spell in hospital, using the date of admission for the first episode and date of discharge for the last episode during the same spell.

All HES admissions were coded with up to 20 separate admission codes to determine the cause of admission. These 20 causes were coded using ICD 10, and were classified as either the primary (the first admission code) or secondary diagnosis (any of the admission codes following the first code) of admission. More detailed information on HES codes is available at http://digital.nhs.uk/hesdatadictionary. The diagnosis code of each admission was extracted from the first episode within the same admission; for the majority of cases in the study dataset, the first episode included the same primary diagnosis code as the subsequent episodes. Whilst this method might underestimate the occurrence of some causes that were coded as secondary diagnoses within any subsequence episodes, the majority of admissions (97.49%) contained only a single spell, therefore, this underestimation is likely to be small.

HES data were used not only to identify hospital activity in detail, but to cross check with hospital information recorded on the YSRCCP to ensure consistent and optimal collection of data on ethnicity and type of treatment received.

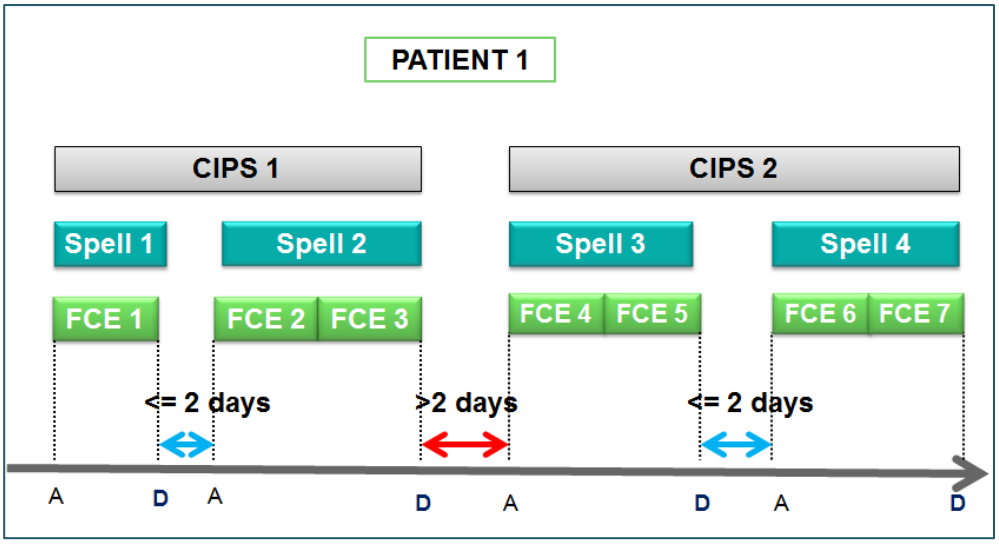


Figure 13: Different classification of hospital admission for the same patient based on HES: finished consultant episodes (FCEs), spells and continuous inpatient spells (CIPs), Abbreviations: A=admission; D= discharge. Data Source: [169]

4.6.3 Comparison group (background population)

This study aimed to assess the excess hospitalisation rate among cancer survivors after completion of treatment with a matched background population. The background population were individuals living in Yorkshire who had at least one hospital episode recorded in HES. Matched data were extracted from HES according to age at admission, sex and year of admission (1997-2011).

4.6.4 Population denominator data

Annual mid-year, age and sex specific population estimates for Yorkshire were extracted from the Office for National Statistics (ONS) (www.statistics.gov.uk) to firstly estimate cancer incidence rates, and secondly to analyse the hospitalisation rates taking account the background population.

The person-years denominator was defined as the time during which cases were believed to be at risk of any hospitalisation. The total person-years during the follow-up period was used to estimate the admission and number of bed days rate ratio and standardised admission rate (hospitalisation rate among the cancer cohort compared to the background population). The follow-up period started from the date of diagnosis to the date of the last admission (1997-2011) and was censored either at the date of death, date last seen on the register, or the end of the study period (31st December 2011) whichever came first.

When estimating the admission duration (length of stay), a person-days denominator was used instead, estimated using the person-years method as above, but with the units re-scaled into days.

A separate calculation of person-years was carried out before and after treatment completion. For example; an individual might be followed-up before completion of treatment, while others might only be followed-up after completion of cancer treatment, i.e. have a linked hospital record or admissions limited to the period after treatment completion. Based on the previous scenario the first case would contribute to the total 'on treatment' person-years calculation, while the second case would contribute to the post-treatment person-years calculation (see Section 4.12.2.1).

Post-treatment cause specific person-years were also estimated, comprising the time (years) from treatment completion until first admission for a specific cause, and censored by date of death, emigration or end of the study period (31st December 2011).

4.7 Data Linkage

All cases extracted from the cancer register were matched to HES data using the patient NHS number, date of birth, sex and address (postcode) for inpatient and outpatient admissions.

4.8 Inclusion criteria

Only cases that were diagnosed between 1996 to 2009 and admitted during the period of 1997 to 2011 were included (Figure 14). Although the cancer register includes cases diagnosed before 1996, their hospital data could be incomplete within the HES. Any cases that were only admitted before their recorded date of diagnosis were eliminated from the study (N=164 cases), because the aim of this project was to look at post-cancer hospitalisation activity. The socioeconomic characteristics for those eliminated cases were not significantly different from the rest of the linked cases in terms of gender, age group, year of diagnosis, ethnicity or deprivation level. However, there was a significant difference in terms of diagnostic group as the majority of the 164 eliminated cases were CNS tumours (40%) and germ cells tumours (24%).

A full description of the number of cases eligible to be included in the study is contained in Figure 14. More than 96% of the registry cases were successfully linked to HES. A sensitivity analysis was done to assess the differences in patient characteristics among linked and non-linked cases to check whether they were broadly similar in terms of their sociodemographic characteristics, including age, sex, year of diagnosis, diagnostic group, ethnicity and deprivation (see Section 5.3.2).

Cases identified in the cancer register that had no recorded admissions were not included in the study analysis, as there was no information regarding the number of admissions, diagnosis on admission or their contribution towards hospital stay. It was not

possible to identify whether there were errors in data linkage, either due to non-matches or linkage mismatches. This could bias the results as some groups tended to be excluded more than others. However, based on a sensitivity analysis, the proportion of cases with no linked hospital record did not vary significantly compared to linked cases (full description in Section 5.3.2).

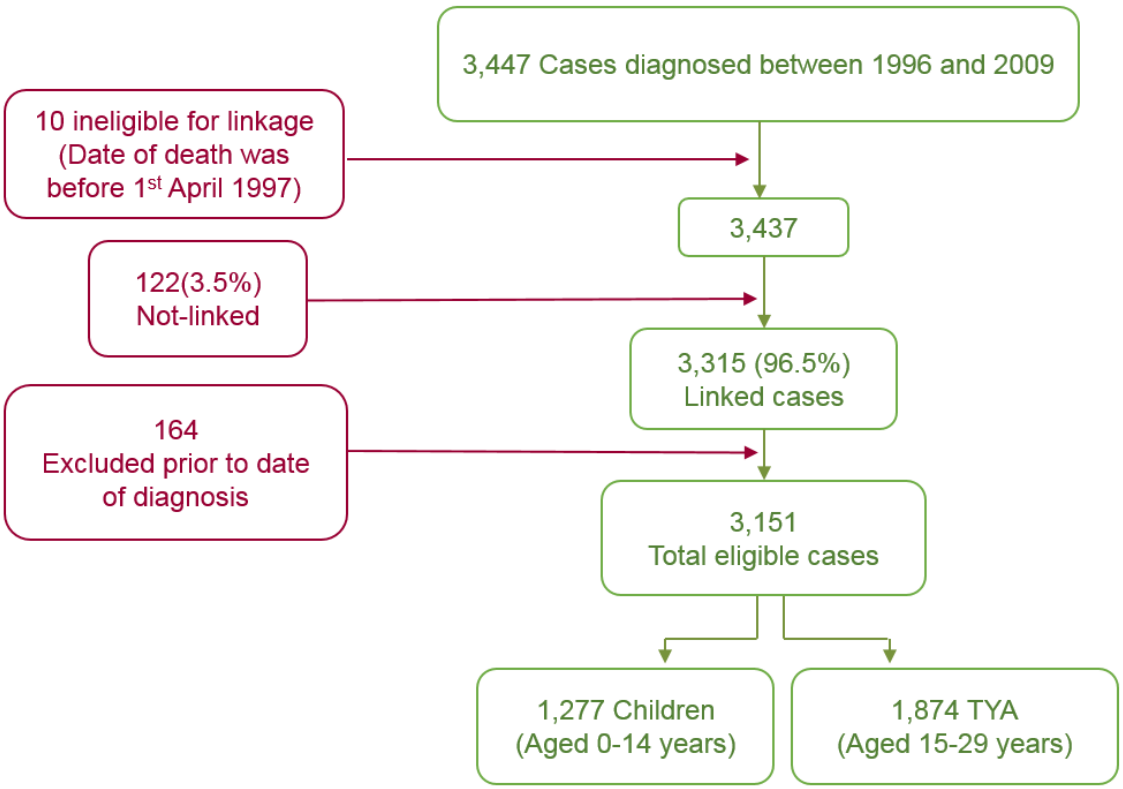


Figure 14: Flowchart representing patient level inclusion criteria

4.9 Data cleaning

Admissions in HES were recorded multiple times for each case, i.e. each case could be admitted more than once during the study period. However, in addition to the true multiple admissions, there were also some duplicate HES admissions. The datasets were cleaned to remove these duplicates, if the following variables were all duplicated: HES ID, episode start date, episode end date, episode order, admission date, discharge date and admission methods as unique identifiers. The HES variable data were coded according to the HES inpatient data dictionary containing a clear definition of codes used in the database [165]. This guidance was used during the cleaning process to ensure consistency and accuracy during recoding and analysis of the data (http://digital.nhs.uk/hesdatadictionary).

4.9.1 Dealing with missing data

The completeness of records in the cancer register was quite satisfactory for age, gender, date of diagnosis, cancer type and deprivation score, with 100% complete records. However, ethnicity and stage were poorly recorded. Details on the alternative methods to overcome this deficiency are fully described in the following sub-sections.

4.9.1.1 Ethnicity

People from minority ethnic groups could have unequal access to healthcare services [170, 171]. In the UK, it has been observed that CYP from minority ethnic groups receive the poorest quality of care [172]. Yorkshire has around 11% of the total South Asians aged 0-29 based on 2001 census data in England [62], where 9% of the total 0-29 years population in Yorkshire were South Asian, as described earlier in Section 4.4. Classifying ethnicity as South Asian vs non-South Asian could provide enough power to compare the pattern of hospital activity by ethnicity, as there was a considerable number of South Asians in West Yorkshire. In contrast, using a detailed classification group could limit the study power in assessing the equity of hospital services by ethnicity. A detailed discussion of the possible ethnicity classifications is provided below.

Information about ethnicity was not accurately or routinely documented in the cancer register, nor in the HES database [62]. To overcome this problem, earlier studies classified patients in the cancer register as South Asian (Pakistani, Indian and Bangladeshi) or non-South Asian (other ethnicity), using the South-Asian Nam Pehchan and/or Name and Group Recognition Algorithm (SANGRA) to allocate ethnicity according to name and additional inspection, done in cases of discrepancy by local experts. SANGRA has sensitivity of 90.5% and specificity up to 97% in allocating cases to the right group [173-175]. In their paper, they used the HES data to cross check the grouping of ethnicity and found that only 2.4% of the cases had disagreement [62]. In addition to the earlier mentioned software, “Onomap” can be used to assign patients to more than 50 categories using an individual’s’ name. The strength of this software is in recognising the patient ethnicity using forename, last name, language and geographical origin. In a study conducted in Scotland, 99% of the cases were successfully linked to specific ethnic groups using Onomap [176]. In their study, the sensitivity of grouping individuals to the right group ranged from 22% for Africans to about 97% for British [176]. The sensitivity in grouping South Asians to the right group was only 75%, however if people who were Muslim from the Middle East were allocated to the South Asian group, the sensitivity analysis increased to 90%. Although this software was not primarily designed for South Asians only, it could be used for extra validation in addition to Nam Pehchan and/or SANGRA. Additionally, this programme has not been used previously to allocate ethnicity extracted from the cancer register in Yorkshire, or UK in cancer registries general.

The cancer register grouped cases into 13 groups based on their ethnic background using 2011 census data (Table 3). The YSRCCYP had a high level of missing ethnicity data (43.5%, n=1,497 out of 3,437), where the cases been recorded with unknown ethnicity.

Therefore, three applications were used to identify ethnicity and cross check with what was recorded in HES. These were: 1) Nam Pehchan [174], 2) SANGRA [173], and 3) Onomap [176]. They allocated cases to suitable ethnicity groups based on their name, as explained earlier. Nam Pehchan and SANGRA identify the South Asian group, hence grouped cases into South Asian or non-South Asian categories (Table 4). Onomap groups ethnicity into 15 ethnic groups, which were then re-allocated into South Asian and non-South Asian categories (Table 5). HES had 13.5% missing ethnicity (n=449 out of 3,315 cases with linked records) and grouped cases into 19 types using the 2001 census. was grouped into 19 categories using the 2001 census. Within HES, ethnicity could be recorded differently for the same person due to multiple admission records. If this was the case, then the most common ethnic group category was selected and these were also then re-grouped into South Asian and non-South Asian categories (Table 6) for comparison with previous epidemiological work in Yorkshire due to the relatively high number of south Asians resident in West Yorkshire [62].

The process used to identify ethnicity was done separately for each source, as presented in Figure 15. Ethnicity was re-allocated into South Asian and non-South Asian groups for each source. Then they were internally analysed for any disagreement in identifying ethnicity between the sources. When cases were identified differently in each source (n=19, 4%), HES datasets were used to determine the ethnicity as they were based on self-reported records.

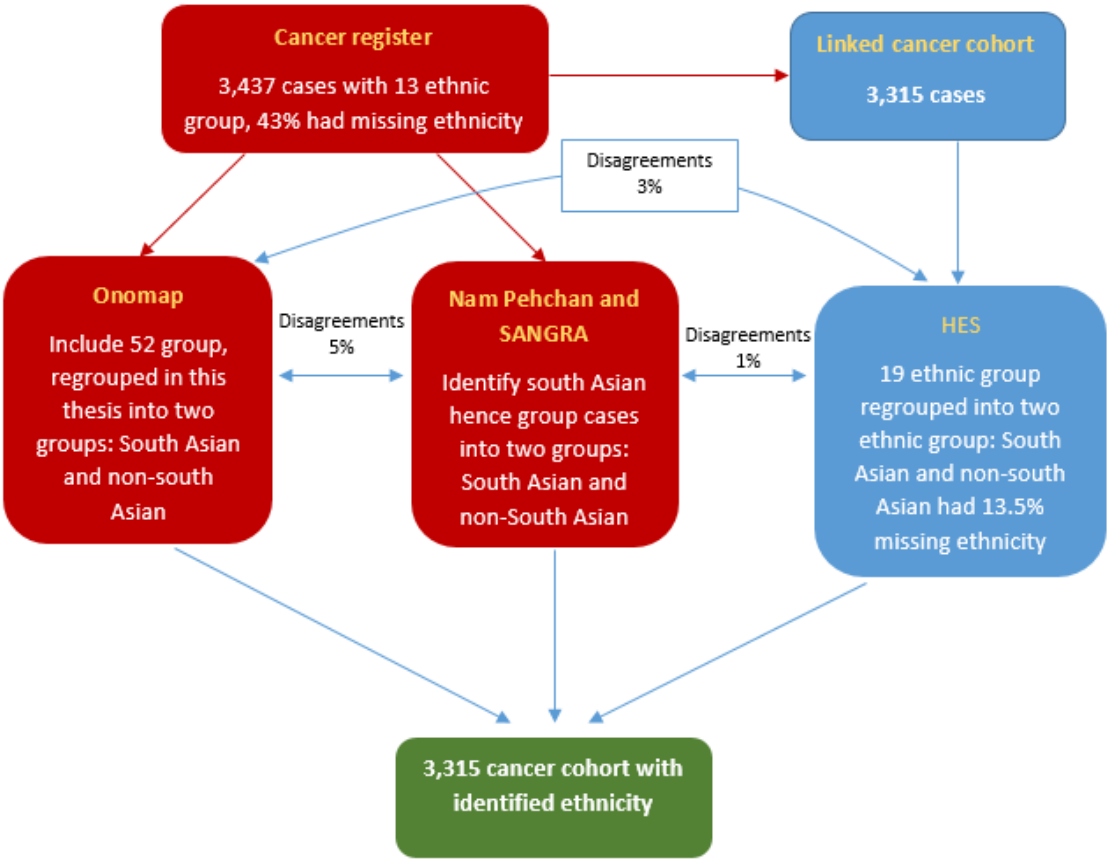


Figure 15: Flowchart of the process done to identify ethnicity

Table 3: The classification of ethnicity in the cancer register (YSRCCYP)

Classification of ethnicity	Re-classification
British	
Any other White background	
White and Black African	
White and Asian	
Any other mixed background	Non-South Asian
Any other Asian background	
African	
Chinese	
Any other ethnic group	
Bangladeshi	
Indian	South Asian
Pakistani	
Not Known	Missing

Table 4: The classification of ethnicity in Nam Pehchan and/or SANGRA

Classification of ethnicity
Non-South Asian
South Asian
Missing

Table 5: The classification of ethnicity in Onomap

Classification of ethnicity	**Re-classification**
Afghanistani	Non-South Asian
African	
Albanian	
Balkan	
Black Southern African	
Castillian	
Celtic	
Channel Islander	
Chinese	
Czech	
Danish	
East Asian & Pacific	
English	
European	
Finnish	
French	
German	
Ghanaian	
Greek	
Greek Cypriot	
Guyanese	
Hispanic	
Hong Kongese	
International	
Iranian	
Irish	
Italian	
Jewish	
Jewish And Armenian	
Maltese	
Muslim	
Nigerian	
Nordic	
Northern Irish	
Polish	
Portuguese	

Classification of ethnicity	Re-classification
Romanian Muntenia	
Scottish	
Sierra Leonian	
Singaporean	
Somalian	
Spanish	
Swedish	
Turkish	
Welsh	
Bangladeshi	
Hindi Not Indian	
India North	
Indian Hindi	
Muslim Indian	South Asian
Pakistani	
Pakistani Kashmir	
Sikh	
South Asian	
Unclassified	
Void	Missing
Not Found	

Table 6: The classification of ethnicity in HES

Classifications of ethnicity	Re-classification
African	
Any other	
Any other Mixed background	
Black	
British	
Caribbean	
Chinese	Non-South Asian
Irish	
Other	
Other Asian	
White	
White and Asian (Mixed)	
White and Black African (Mixed)	
Bangladeshi	
Indian	South Asian
Pakistani	
Not given	
Not known	Missing
Not stated	

4.9.1.2 Staging

Stage is a tool used to allocate tumours into different groups to identify how advanced the disease is based on the biological nature of the tumour around the time of presentation or diagnosis. This includes the location of the primary tumour, the size of the tumour, whether the tumour has metastasised to other organs or spread to lymph nodes. For some cancers, it is important to know how the cancer cells differentiate from the normal cells and are graded according to the level of differentiation. For example, grade I refers to low grade tumours where the cancer cell is similar to normal cells whilst grade IV refers to high grade tumours when the cell is completely different for the normal cells. It is widely used for clinical purposes to identify disease severity and subsequent planning of treatment.

There are many different staging systems used depending on cancer type and these have changed over time due to developments in diagnostic accuracy and biological characterisation of tumours. Information on stage was known to be inconsistently recorded within the YSRCCYP and this also varied by cancer type [49]. In this study for all cancers combined, 1,653 (53%) survivors had data on stage missing and this ranged from 16% (leukaemia) to 100% (bone tumours) by cancer type. Thus, there was no consistent method available to stage all tumours consistently across the various cancer types. CNS tumours and haematological tumours often use a proxy such as grade and white blood cell count (wcc) respectively , where the higher the grade and wcc, the greater the disease severity [49]. For CNS tumours, cancerous cells are unlikely to spread to other organs and it is the size of the tumour which is most important in differentiating stage [177]. Therefore for CNS tumours grade was used rather than stage based on the World Health Organisation (WHO) grading.

Grade was used to estimate the treatment duration for cases with CNS tumours. That was done by classifying cases to low grade and high grade tumours using the WHO grading system; low grade tumours were identified as cases with grade I and II, while high grade tumours were cases with grade III and IV. Based on agreement with clinical collaborators, it was suggested that cases with low-grade glioma had the longest treatment duration of 18 months, as they needed to be under supervision to monitor the change in the tumours, whereby individuals might go more than a year without receiving treatment until the prognosis was confirmed. Those with high-grade glioma had the shortest treatment duration, especially for cases with radiotherapy alone lasting around six months. These treatment durations are explained in detail in Table 9. 276 out of 463 CNS survivors had their grade identified using the cancer register (168 low grade and 62 high grade), while 187 cases (40%) had missing grades. Those were identified

individually using the morphological code , to impute grade and their treatment durations updated accordingly [178].

Stage is an important variable and is likely to affect the pattern of hospital admissions. Patients with worse prognosis (stage/grade IV) might have multiple hospital admissions compared to cases with better prognosis (stage/grade I). However, due to the high percentage of missing data and the inconsistent classification of stage or grade, this variable was not included in the regression modelling. Nonetheless, other variables such as relapse status and type of initial treatment, that could determine disease severity were considered for inclusion in the modelling. Stage is likely to be highly correlated with type of initial treatment, especially for CNS tumours, where those with high-grade CNS tumours treated with radiotherapy have shorter treatment durations than cases with low-grade CNS tumours treated with radiotherapy. Therefore, including stage and type of initial treatment in the model was not valid as it breached one of the negative binomial conditions, which is the independence of all the predictor variables.

4.10 Ethical approval and data security

Ethical approval for this project was already in place because it was included as part of an ongoing research programme for the YSRCCYP: (MREC 0/3/1) investigating variation in hospital activity. The approval allows the processing of patient identifiable data without consent for research purposes through an exemption from the Health Research Authority Confidentiality Advisory Group (CAG 1-07(b)/2014).

This project relied on the extraction of data on hospital activity for cancer patients aged 0-29 from HES. Approval to work with HES data was provided by the Health and Social Care Information Centre [165], Data Access Advisory Group – DAAG reference: OC/HES/015, as part of the work approved within the YSRCCYP.

To preserve statistical power and avoid disclosing any patient identifiable information, each cancer group was only studied in detail when there were more than 50 cases. The numbers in the tables were suppressed when there were fewer than five cases. All data were analysed within a secure server environment in the School of Medicine at the University of Leeds where only authorised registry personnel had access to the data and networked PCs.

4.11 Demographic and clinical characteristics

4.11.1 Proxy of deprivation

The frequency of hospital admissions and length of stay might vary due to socioeconomic status; people in the most deprived areas have been previously shown to have higher hospitalisation use among long-term survivors [101]. Therefore, hospitalisation usage was assessed in relation to deprivation. There were several proxies of deprivation Carstairs [179], Townsend [180] and Index of Multiple Deprivation (IMD) [181] that were previously used in childhood cancer epidemiological studies. Each uses certain components to estimate a deprivation score. Townsend is an area-based deprivation measurement using the following indices: unemployment, non-car ownership, non-home ownership and household overcrowding within a small area measure, such as electoral ward or super-output area [19]. The IMD [181] has the limitation of including health data that could overestimate the relationship between deprivation and health. To provide a comprehensive analysis, and for the sake of comparability with other studies conducted in the Yorkshire study region, the Townsend score was used as a proxy of deprivation [48, 127]. The use of an area-based measure could lead to ecological fallacy problems, as area-level associations may not be representative of those at an individual level because of the aggregation of data and loss of information [19]. To avoid that potential bias or at least to reduce its effect, the smallest area-based measure was used – 'lower super output area' – which constitutes a minimum of 1,000 people and a mean of 1,500 people in England [182]; this could reduce the loss of individual level information. Deprivation scores were derived from the 2001 census and then categorised into five groups from the least to the most deprived based on the distribution of scores in Great Britain.

4.11.2 Date of diagnosis

To remain consistent in identifying accurate diagnosis dates among diagnostic groups, a hierarchy exists, ordered from lowest to highest priority, taken from the European Network of Cancer Registries [183, 184] (Box 1). The YSRCCYP register follows this guidance to determine an accurate diagnosis date, which I used within this thesis. The date of diagnosis from the registry was based on manual scrutiny of the original medical records, and adhered to rules on defining the diagnosis date set out by national cancer registration guidelines, also adopted and documented by the European Network of Cancer Registries [185]. Diagnosis dates were primarily determined via the date recorded on the histopathology report from when the biopsy specimen was taken. Otherwise, the earliest recorded date at which the diagnosis was confirmed via radiology (computed topography or magnetic resonance imaging) or other clinical confirmation was taken. Nevertheless, there may be some measurement error associated with the registry recorded data of diagnosis based upon this method, although any impact on analyses is likely to be mitigated due to regular cross-checks having been carried out

between the YSRCCYP, other regional specialist childhood registries, the National Registry for Childhood Tumours and National Cancer Registration Service [183]. The manner in which some tumours are diagnosed through surgical excision and the delays associated with confirmation of the date of diagnosis, some cases will have begun treatment or would have been hospitalised before the recorded date of diagnosis in the cancer register, thus this may result in an underestimation of the real hospital burden for some cases.

Box 1: The hierarchy of defining date of diagnosis based on the European Network of Cancer Registries: [171].

In the order of declining priority:

1. Date of first histological or cytological confirmation of this malignancy (with the exception of histology or cytology at autopsy). This date should be, in the following order:
   (a) date when the specimen was taken (biopsy)
   (b) date of receipt by the pathologist
   (c) date of the pathology report
2. Date of admission to the hospital because of this malignancy.
3. When evaluated at an outpatient clinic only: date of first consultation at the outpatient clinic because of this malignancy.
4. Date of diagnosis, other than 1, 2 or 3.
5. Date of death, if no information is available other than the fact that the patient has died because of a malignancy.
6. Date of death, if the malignancy is discovered at autopsy.

4.11.3 Classification of ethnicity

As described earlier in Section 4.9.1.1, cases were grouped into South Asian and non-South Asians as those groups were appropriate for the study population.

4.11.4 Identification of treatment modality and date of completion

The Department of Health's Cancer Reform Strategy emphasises the importance of providing high-quality data on cancer outcomes and the survival population, to optimise health services planning to address their needs. However, the Department of Health found that data completion for stage of disease and treatment was inconsistent in the UK [186]. Cancer treatment information for this study was extracted from the YSRCCYP and HES. In the current study, we were interested in assessing admissions after date of diagnosis of primary cancer, and separately before and after date of initial treatment completion. In the YSRCCYP, the type of treatment (chemotherapy, radiotherapy, surgery, bone marrow transplant (BMT)) were stored in a separate database table and linked to each tumour registration using patient ID, type of tumour and date of diagnosis. However, this limited the ability to identify the type of initial treatment or the first line treatment, e.g. certain cases might have planned to receive chemotherapy alone,

however, the tumour may still have been present at the end of the chemotherapy regimen and therefore further treatment would be prescribed.

As described in Section 4.6.2, each NHS healthcare provider in the UK is funded based on the delivery of their services, a policy known as PbR [187]. The PbR system is sensitive to case mix, such as type of treatment provided, length of stay, age of patient and other clinical and demographic characteristics of the patient. The completeness of the PbR report is the responsibility of each NHS provider, with data uploaded on a monthly basis to Healthcare Resource Groups (HRG). These reports are held by the Health and Social Care Information Centre (HSCIC), with the data available for research purposes subject to appropriate legal and regulatory approvals. HES are acknowledged to accurately represent the level of surgical procedures. The accuracy and completeness of recording of treatment within both the cancer register and HES has been analysed. It has previously been found that the recording of major surgery was considerably high, while radiotherapy and chemotherapy were poorly recorded in HES [8]. Therefore, HES was used to cross-validate primarily the recording of surgical procedures in the cancer register, especially for patients with no record of treatment within the cancer register.

Further validation of those from the cancer register with no record of treatment were checked against medical records and the original cancer register data collection notes. Results showed that of those with no record of treatment in the cancer register (n= 375), after validation a two-third (~70%) of these were accurately recorded as having received no actual treatment.

4.11.4.1 Identification of initial treatment

For surgery, based on clinical expertise, only major surgical interventions related to treatment were included. Supportive and diagnostic purpose surgeries, such as biopsies and exploratory surgeries for diagnostic purposes, or gastro-enterostomy or catheter insertion for supportive purposes, were not considered to be cancer-related major surgeries. A full list of diagnostic supportive and therapeutic surgeries is included in Appendix B. In HES, the operation codes were used to classify surgeries by surgery site [188]. The list of potential curative cancer-related surgeries was identified using the National Cancer Intelligence Network Major Resection Report [189].

Another major surgical list was generated based on current operations conducted on the study population, and was inspected and approved by a local consultant paediatric and adolescent haematologist. Both lists were cross-checked; a list of the surgical operations included in the study can be found in Appendix B.

The date of treatment was documented in the cancer register, however each case might have multiple dates of treatment, in relation to primary or secondary tumour diagnoses,

thus the initial date was defined as the earliest date of delivery of treatment in cases with a single modality. The date of initial treatment for a patient with complex modality was not reliable, as they had several initial dates for each modality (chemotherapy, radiotherapy and surgery). In that case, a proxy table was created to estimate the expected time point where the treatment was considered as initial, i.e. planned as the first-line treatment based on discussions with clinical experts. Thus, Table 7 was created to summarise different treatment scenarios. This table was used when cases had the recorded date of each treatment modality. When cases had no record of treatment, the date of diagnosis was used. The dates for chemotherapy, radiotherapy and surgery were considered as initial therapy if they occurred during the predefined time points set out in Table 7 for each cancer diagnostic group and type of treatment modality. For CNS tumours, it was separated by histological type: low-grade tumour and high-grade tumour [111], as described earlier.

In cases of discrepancy in the coding of treatment between the cancer register and HES in terms of date of treatment or type of treatment, the date chosen was the earliest date recorded as any following dates could relate to the continuation of subsequent treatment modalities. When there were discrepancies in documentation of treatment type, e.g. surgery alone in the cancer register and chemotherapy alone in HES, both treatments were assigned to cases if they were within the predefined initial treatment duration time period. All possible combinations of treatments from both datasets are illustrated in Table 8. In the study dataset treatment modality was grouped into eight groups (Table 9).

Table 7: Classification tool used in identification of initial treatment

Diagnostic group	Gender	Treatment duration from date of start of chemotherapy or date of diagnosis if patient didn't receive chemotherapy for cases treated with radiotherapy and/or surgery
Leukaemia		
ALL	Female	24 months
ALL	Male	36 months
AML	Both	6 months
Other leukaemia		24 months
Lymphoma		
Non-Hodgkin lymphoma	Both	6 months
Hodgkin lymphoma	Both	12 months
Other lymphoma		12 months
CNS		
Low grade	Both	18 months
high grade	Both	6 months if radiotherapy alone / otherwise 12 months
Neuroblastoma	Both	3 months if surgery alone / otherwise 18 months
Renal tumour	Both	12 months
Bone tumour	Both	12 months
STS	Both	3 months if surgery alone / otherwise 12 months
Germ cell tumour	Both	3 months if surgery alone / otherwise 8 months

Abbreviations: ALL= Acute lymphoblastic leukaemia; AML= Acute myeloid leukaemia; CNS= Central nervous system; STS= Soft tissue sarcoma.

Table 8: All possible combinations of treatment modality from the cancer register and HES

Example modality in one of the data sources (HES or register)	Example modalities in the other data source	Final assigned treatment modalities
Chemotherapy alone	Radiotherapy alone/ Chemotherapy and radiotherapy	Chemotherapy and radiotherapy
	Surgery alone/ Chemotherapy and surgery	Chemotherapy and surgery
	Radiotherapy and surgery	Chemotherapy, radiotherapy and surgery
	Chemotherapy, radiotherapy and surgery	Chemotherapy, radiotherapy and surgery
Radiotherapy alone	Chemotherapy alone/ Radiotherapy and surgery	Chemotherapy and radiotherapy
	Surgery alone/ Radiotherapy and surgery	Radiotherapy and surgery
	Chemotherapy and surgery	Chemotherapy, radiotherapy and surgery
	Chemotherapy, radiotherapy and surgery	Chemotherapy, radiotherapy and surgery
Surgery alone	Chemotherapy alone/ Chemotherapy and surgery	Chemotherapy and surgery
	Radiotherapy alone/ Radiotherapy and surgery	Radiotherapy and surgery
	Chemotherapy and radiotherapy	Chemotherapy, radiotherapy and surgery
	Chemotherapy, radiotherapy and surgery	Chemotherapy, radiotherapy and surgery
None recorded	Any other treatment combination	Other treatment combination

Table 9: The classification code for the treatment variable

Classification of treatment	Code	Justifications
Chemotherapy alone	1	
Radiotherapy alone	2	
Surgery alone*	3	
Chemotherapy and radiotherapy	4	
Chemotherapy and surgery	5	
Radiotherapy and surgery	6	
Combination of all	7	
Not recorded	8	No record of treatment

* For the surgery variable, diagnostic aid procedures were not considered to be a cancer-related surgery.

4.11.4.2 Estimated date of treatment completion

To answer the main research question of assessing the patterns of hospital admissions during the post-treatment phase, it was essential to know the date when treatment was completed. However, this information was not consistently available either in the cancer register or the HES dataset. Consequently, the approximate date of treatment completion was inferred based upon clinical knowledge (group of senior local paediatric and adolescent haematology and oncology consultants), using the following variables: diagnostic group, gender, type of initial treatment, whether the patient had a BMT or had ever relapsed. Based on agreement with clinical experts, a proxy indicator for duration of treatment in months was generated using the aforementioned variables (Table 10).

Table 10: Expected duration of treatment completion according to diagnostic group, gender, bone marrow transplant and relapse status

Diagnostic group	Gender	Treatment duration from start of chemotherapy, radiotherapy or surgery (from the latest date of treatment start date)	Bone marrow transplant (from date of transplant)	Ever Relapsed (from date of relapse)	Proxy date of end of treatment
Leukaemia			12 months	12 months	The latest date of end of treatment
ALL	Female	24 months			
ALL	Male	36 months			
AML	Both	6 months			
Other leukaemia		24 months			
Lymphoma					
Non-Hodgkin lymphoma	Both	6 months			
Hodgkin lymphoma	Both	12 months			
Other lymphoma		12 months			
CNS					
Low grade	Both	18 months			
High grade	Both	6 months if radiotherapy alone / otherwise 12 months			
Neuroblastoma	Both	3 months if surgery alone / otherwise 18 months			
Renal tumour	Both	12 months			
Bone tumour	Both	12 months			
Soft tissue sarcoma	Both	3 months surgery alone / otherwise 12 months			
Germ cell tumour	Both	3 months surgery alone / otherwise 8 months			

Abbreviations: ALL=Acute lymphoblastic leukaemia; AML= Acute myeloid leukaemia; CNS=Central nervous system

4.11.4.3 Relapse status

The follow-up process described in Section 4.6.1 outlines how relapse disease was ascertained. Relapse was defined as recurrent disease regardless of the site [190].

There could be more than one relapse event per patient of course, although this study focused only on the first relapse after primary diagnosis as the management of treatment differs after the second relapse, resulting in a biased assessment of health burden. Additionally, only a quarter of those who relapsed had more than one event, hence limiting the ability to study this group separately.

4.11.4.4 Bone marrow transplant (BMT)

Along with chemotherapy, radiotherapy and surgery, some cases require a further clinical intervention such as BMT. BMT is one of the treatment protocols available for chronic illness, limited mainly to AML patients affected by loss of bone marrow cells due to intensive treatment, therefore necessitating BMT. After the transplantation, the patient might need up to 12 months for their white blood count and immune system to return to normal levels.

Information on BMT was recorded in the cancer register as one of the treatment modalities. In addition, HES data were cross-checked using the three digit Classification of Interventions and Procedures (OPCS) code version 4.5 [46], and from the main paediatric and adolescent oncology department at Leeds Teaching Hospitals NHS Trust where treatment was administered during admission. Figure 16 presents the sources and codes used to identify cases with BMT. The list of BMT operations extracted from the cancer register and HES data was cross-checked against the electronic records held by the Leeds General Infirmary for all such procedures carried out at the only PTC in the region for CYP.

The date of the BMT was extracted from HES and compared to the date of diagnosis to check whether the transplant occurred after diagnosis or close to the date of diagnosis, hence ensuring that the transplant was related to the primary cancer and not due to another chronic diseases or second malignancy.

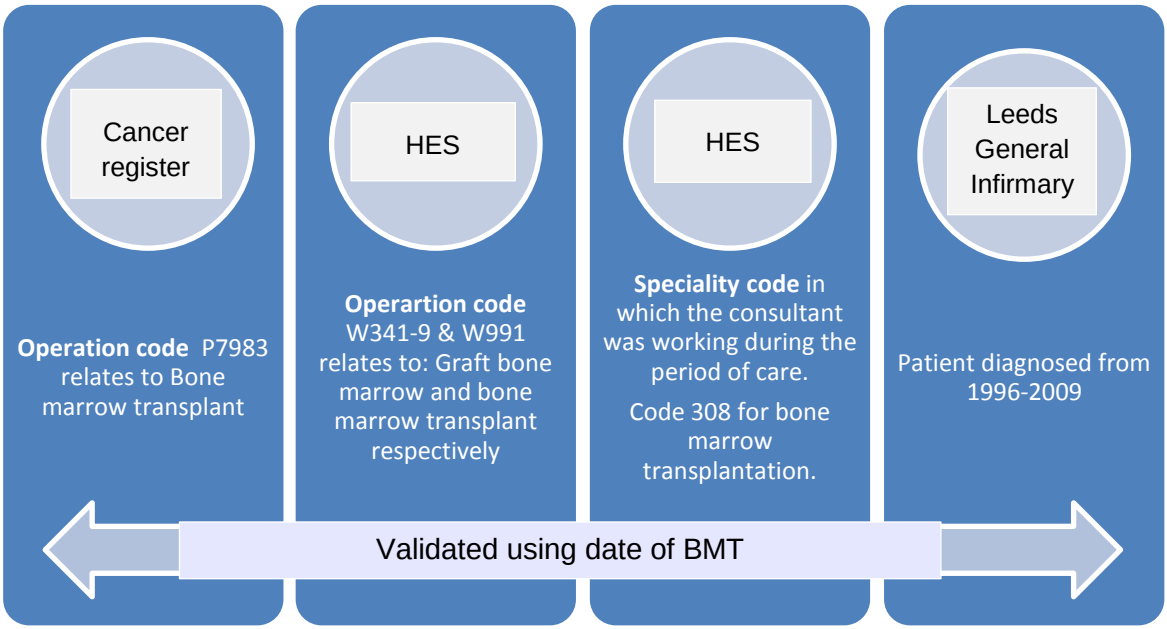


Figure 16: Validation of bone marrow transplant

4.11.5 Type of admission

For certain parts of the analysis (Section 6.2.1.5), the type of admission was recorded to compare the results with previously published hospital activity reports in the UK. The types of admission were grouped as either 'planned' (elective) or 'unplanned', as identified using the HES data dictionary (see Table 11).

Table 11: Classification code for admission method

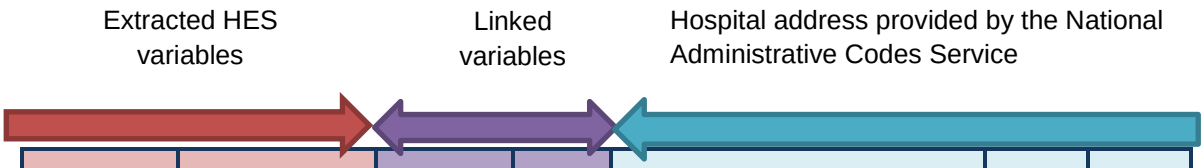
Admission method		Code	Code descriptions
Planned		11	From waiting list
		12	Booked
		13	Planned
Unplanned	**Emergency**	21	Via Accident and Emergency (A&E)
		22	Via general practitioner
		23	Via Bed Bureau
		24	Via consultant outpatient clinic
		28	Other means
	Maternity	31	Baby was delivered after the mother's admission
		32	Baby was delivered before the mother's admission
	Others	81	Transfer of any admitted patient from another hospital provider other than in an emergency
		82	Other: babies born in healthcare provider
		83	Other: babies born outside the healthcare provider, except when born at home
		84	Admission by the admission panel of an HSPH; patient not entered on the HSPH
		89	From the admissions waiting list of an HSPH
	Not known	98	Not applicable
		99	Not known

4.11.6 Place of care during the admission period and proportion of specialist care

The pattern of admissions might vary depending on the type of hospital where cancer was diagnosed, or where the treatment was delivered, as explained earlier in Chapter 3, Section 3.3.4.1, and also on whether the services were delivered at specialist or non-specialist hospitals. Consequently, it was essential to identify the hospital where services were delivered before classifying the hospital type (specialist or not).

Identifying the main place of care for cancer patients, especially CYP, was difficult. Patients could be diagnosed in one NHS trust, but receive treatment at another, or they could be diagnosed and receive their initial treatment in the same trust, but during their treatment period, care might be delivered by a different trust. The relationship between place of care and the survival rate among patients with colorectal cancer in the Northern and Yorkshire region was previously studied, and found that around 90% of patients were receiving care in the same trust where they were diagnosed; whilst only 75% maintained care from the same setting throughout the treatment journey [19].

To identify the hospital where the patient received care during the admission period, individual hospital names were identified from the HES admission records based on the HES inpatient data dictionary [165] (Figure 17), and then flagged within the dataset as representing a specialist centre (either age or tumour-specific) based on the lists in Table 12 and Table 13**.** This list was extracted from three online sources: The Children's Cancer and Leukaemia Group [53], the Teenage Cancer Trust [131] and Cancer Support for the Young (CLIC Sargent) [191]. Furthermore, these were individually checked though the hospital websites to identify age boundaries. These lists represent specialist centres available for CYP up to 2013, when data analysis began, ensuring accurate allocation of cases based on the level of specialist care, by appropriately identifying the type of hospital where they were admitted and treated.



Yctr_id	Admidate	Procode	Organisation code	Name	National grouping	High level geography
990XX	26/10/19XX	RR813	R1A	Worcestershire Health And Care NHS Trust	Y55	Q53
09AXX	05/08/20XX	RAE00	R1C	Solent NHS Trust	Y57	Q70
2003XX	07/07/20XX	RR801	R1D	Shropshire Community Health NHS Trust	Y55	Q60
2006XX	30/08/20XX	RR801	R1E	Staffordshire And Stoke On Trent Partnership NHS Trust	Y55	Q60

Abbreviations: Admidate is the admission date; Procode is the provider code as described in detail in http://digital.nhs.uk/hesdatadictionary.

Figure 17: Visual example of the method used to identify the name of the healthcare providers

Table 12: List of CYP cancer treatment centres (hospitals) with location and age boundaries in UK and Ireland in 2013

Hospital name	City	Age boundaries
Royal Aberdeen Children's Hospital	Aberdeen	0 to 16 years
Royal Belfast Hospital for Sick Children	Belfast	0 to 16 years
Birmingham Children's Hospital	Birmingham	0 to 12 and 13-18 years
Queen Elizabeth Hospital Young Persons Unit	Birmingham	16 to 18 years
Royal Orthopaedic Hospital	Birmingham	13 to 18 years
Bristol Royal Hospital for Children	Bristol	0 to 10 and 11 to 16 years
Children's Hospital for Wales (CHW)	Cardiff	0 to 20 and 13-24 years
Addenbrooke's Hospital	Cambridge	14 to 24 years
Royal Hospital for Sick Children	Edinburgh	0 to 12 and 13 to 16 years
Western General Hospital	Edinburgh	16 to 24 years
Beatson West of Scotland Cancer Centre	Glasgow	16 to 24 years
Royal Hospital for Sick Children (Yorkhill)	Glasgow	0 to 12 and 13 to 16 years
Castle Hill Hospital	Hull	18 to 24 years
Leeds General Infirmary	Leeds	0 to 12 and 13-18 years
St James's University Hospital Young Adult Unit	Leeds	17 to 24 years
Leicester Royal Infirmary	Leicester	13 to 24 years
Alder Hey Children's Hospital	Liverpool	0 to12 and 13-19 years
University College Hospital	London	0 to 12 and 13 to 24 years
The Royal Marsden	London	0 to15 and 16-24 years
Royal Manchester Children's Hospital	Manchester	0 to 12 and 13 to 24 years

Hospital name	City	Age boundaries
The Christie Hospital	Manchester	16 to 24 years
The Freeman Hospital	Newcastle	18 to 24 years
The Great North Children's Hospital	Newcastle	13 to 19 years
Royal Victoria Infirmary	Newcastle Upon Tyne	0 to 13 years
Queen’s Medical Centre	Nottingham	0 to 18 and 19 to 24 years
John Radcliffe Hospital	Oxford	Birth to18 years
The Children's Hospital Sheffield	Sheffield	Birth to 16 years
Royal Hallamshire Hospital	Sheffield	16 to 24 years
Weston Park Hospital	Sheffield	16 to 24 years
Southampton General Hospital	Southampton	0 to15 and 16-24 years
Royal Marsden Hospital	Surrey	16 to 24 years
The Clatterbridge Cancer Centre	The Wirral	16 to 24 years

Table 13: Other specialist hospitals (tumour specific) with cancer-specific expertise

Hospital name	Cancer-specific expertise
Charing Cross Hospital	CNS tumours
James Cook Hospital	CNS tumours
Kings College Hospital	CNS tumours
National Hospital for Neurology and Neurosurgery	CNS tumours
Queens Hospital Romford	CNS tumours
Royal Free Hospital	CNS tumours
Royal Preston Hospital	CNS tumours
Royal Stoke University Hospital	CNS tumours
Salford Royal Hospital	CNS tumours
St George’s Hospitals, Tooting	CNS tumours
The Walton Centre	CNS tumours
University Hospital (Coventry)	CNS tumours
Great Ormond Street Hospital	CNS tumours
Hull Royal Infirmary	CNS tumours
Derriford Hospital	CNS tumours and soft tissue sarcoma
Churchill Hospital	Soft tissue sarcoma
City Hospital	Soft tissue sarcoma
Frenchay Hospital (diagnostic surgery)	Soft tissue sarcoma
Manchester Royal Infirmary	Soft tissue sarcoma
Royal Devon and Exeter Hospital	Soft tissue sarcoma
Royal Liverpool Hospital (diagnostic and surgery)	Soft tissue sarcoma
Nuffield Orthopaedic Centre, Oxford	Bone tumours
Royal National Orthopaedic Hospital, Stanmore	Bone tumours
Royal Orthopaedic Hospital, Birmingham	Bone tumours
The Robert Jones & Agnes Hunt Orthopaedic Hospital, Oswestry	Bone tumours

The proportion of specialist care received by the patient was calculated in two ways. The first method attempted to calculate this proportion based on the number of admissions to specialist cancer centres (Outcome 1) and the second method was based upon the number of days spent in specialist centres in each admission/spell (Outcome 2)

Specialist cancer centres, as explained earlier in the introduction chapter, could represent either age specific (children and TYA PTC) or tumour specific centres, and reflect levels of high quality care. It was found that those diagnosed with cancer aged 15-24 years and treated in specialist centres had better survival rates than TYA cases with limited access to specialist services [10]. However, in this study the proportion of specialist care was estimated using hospital stay only, i.e. the proportion of stay in specialist units compared to the overall length of time spent in hospital. Within this thesis, two different measures of hospital burden were used: frequency of hospital admissions and length of stay. This was to take into account individuals who may have fewer specialist admissions but spent extended periods of time in specialist units. Both methods were used when carrying out regression modelling to examine factors which influenced hospitalisation, in order to identify the independent effects of specialist care based on the study outcome: hospital admission or length of stay.

Outcome 1: Proportion of specialist care based upon the number of admissions

$$\textbf{Proportion of specialist care admissions} = \frac{\text{Total number of specialist care admissions per patient}}{\text{Total number of admissions per patient}}$$

Outcome 2: Proportion of specialist care using number of days

$$\textbf{Proportion of specialist care days} = \frac{\text{Total number of days in specialist units per patient}}{\text{Total number of days spent in hospital per patient}}$$

The proportion of admissions was then grouped into three categories, firstly to aid interpretation, and secondly, to compare the results to the published literature that assessed the impact of levels of specialist care on cancer outcomes [8] (Table 14).

Table 14: Classification of levels of specialist care

Code	Category label	Proportion of specialist care
1	Limited specialist care	<30%
2	Some specialist care	30-60%
3	Mostly specialist care	>60%

4.11.7 Follow-up period

As described earlier in Section 4.6.4 the follow-up period was calculated based on the linked data from the date of diagnosis until date of death, date of immigration, or the end of the study period (31st December 2011) whichever occurred first. The follow-up period was further categorised into two phases:

1. On treatment phase: from date of diagnosis to date of treatment completion (the estimated date of treatment completion in Section 4.11.4.2), date of death, date of loss of immigration or date of the end of study period whichever occurs first.
2. Post-treatment phase: date of treatment completion to the date of end of follow-up (date of immigration, death or 31 December 2011, whichever occurred first). The follow-up period after treatment completion was subdivided further by: the censoring point from date of treatment completion: 0-2 years after date of treatment completion, 3-4 years after date of treatment completion, 5-7 years after date of treatment completion, $\geqslant$ 8 years after treatment completion. These were established to classify the pattern of admissions into 'short', 'median' and 'long term' follow-up periods.

4.12 Statistical methods

4.12.1 Cancer incidence rates

The incidence rates for all cancers overall and by main diagnostic group were assessed, using age and sex standardised incidence rates per 1,000,000 people and 95% confidence intervals using annual mid-year, age- and sex-specific population estimates . Additionally, the temporal trends in cancer incidence by year of diagnosis were assessed.

4.12.2 Linked study population

The study population was described according to clinical and patient demographics by comparing the distribution of cancers by age at diagnosis, sex, year of diagnosis, ethnicity, and deprivation for linked and non-linked cases using the Chi-squared test for categorical data, *t*-test for normally distributed continuous variables and the Mann-Whitney U-test [192] for non-normally distributed variables. This was done to check for any significant selection bias.

One of the study objectives was to check the completeness in documenting the initial type of treatment in the cancer cohort and HES datasets. Therefore, the distribution of cases by type of treatment and data source was calculated comparing data extracted from the cancer register and HES. Similarly, the number and percentage of cases treated with BMT and the number of cases experiencing a relapse were calculated and compared by cancer type. Furthermore, the number of admissions was compared by

level of specialist care and age at diagnosis. These were done to describe the management of the cancer cohort by cancer type, age, type of initial treatment and disease severity. The results are presented in Chapter 5.

4.12.2.1 Estimating the number and rates of admissions and bed days

The objective was to assess the frequency of hospital admissions and number of days spent in hospital among CYP by comparing the rates of hospital admission for each cancer type during two time periods: on treatment and post-treatment. This was carried out to estimate the burden of health among the cancer cohort from the date of diagnosis, and additionally, after treatment completion when patients are considered to be free of cancer. Furthermore, this should give an insight into the use of hospital services among short- (treatment phase), medium- (immediately after treatment completion) and long-term survivors (more than three years after treatment completion).

The rate of admission was analysed for all cancers combined and for main diagnostic groups, taking into account the number of years of follow-up. The rates were broken down by demographic characteristics such as age, sex, ethnicity and deprivation.

In the current thesis, two measures of hospital activity were considered:

1. Hospital admission rates – separated into inpatient and outpatient rates. Admission rates (per person per year, as described in Section 4.6.4) were estimated for all cancers combined and by main diagnostic group according to patient demographics and clinical characteristics.
2. Number of days spent in hospital (inpatient) was defined as the total number of bed days during acute hospitalisation per 100 person per day from the date of admission until discharge.

The following examples describe the method used to estimate the hospital rate per patient by identifying the number of admissions per patient and the number of follow-up years since diagnosis until the last admission or censoring (Table 15 and Figure 18).

In Table 15 each row represents a single case. Numbers of admissions were calculated at three time points: the first time period was calculated from the date of diagnosis until date of treatment completion; the second period is from the 1st admission after treatment completion to the last admission during the study period (31st December 2011); the third period is the complete follow-up period from date of diagnosis until the end of the study period (31st of December 2011).

- Column A in Table 15 represents the number of admissions in the three main time periods: total follow-up period from diagnosis, on treatment phase and post-treatment period. The pink colour represents the further breakdown of the post-

treatment period into distinct epochs (<3, 3-5, 5-7 and >8 years after treatment completion).

- Column B represents the number of years patients were followed-up from the date of diagnosis until the end of the study follow-up period (31st December 2011) or censored due to death, emigration or loss to follow-up.
- Column C represents the admission rate using the Outcome 3 formula.

Table 15:Example 1: estimating the hospital admission rate based on the number of admissions

Patient ID	(A) Number of admissions							(B) Follow-up period (years)							(C) Hospital admission rate (admissions per year) (Outcome3*)					
	Total	**On treatment**	<3 post treatment	3 to <5 post-treatment	5 to <8 post-treatment	>=8 post-treatment	**Post-treatment**	**Total**	**On treatment**	<3 post treatment	3 to <5 post-treatment	5 to <8 post-treatment	>=8 post-treatment	**Post-treatment**	**On treatment**	<3 post-treatment	3 to <5 post-treatment	5 to <8 post-treatment	>=8 post-treatment	**Post-treatment**
1	**16**	**2**	14	0	0	0	**14**	2.44	**1.09**	1.35	0.00	0.00	0.00	**1.35**	**1.84**	10.35	0.00	0.00	0.00	**10.35**
2	**7**	**0**	0	7	0	0	**7**	4.58	**0.62**	2.99	0.97	0.00	0.00	**3.96**	**0.00**	0.00	7.20	0.00	0.00	**1.77**
3	**14**	**0**	12	2	0	0	**14**	4.00	**0.99**	2.99	0.02	0.00	0.00	**3.01**	**0.00**	4.01	82.06	0.00	0.00	**4.64**
4	**3**	**0**	2	0	1	0	**3**	5.74	**0.68**	2.99	1.99	0.09	0.00	**5.07**	**0.00**	0.67	0.00	11.76	0.00	**0.59**
5	**8**	**2**	3	0	2	1	**6**	10.55	**1.48**	2.99	1.99	2.99	1.10	**9.07**	**1.35**	1.00	0.00	0.67	0.91	**0.66**
6	**19**	**2**	10	2	3	2	**17**	10.62	**1.05**	2.99	1.99	2.99	1.59	**9.56**	**1.90**	3.34	1.01	1.00	1.26	**1.78**

Blue represents the entire follow-up period, green the on treatment and post-treatment periods, and pink the breakdown of post-treatment follow-up.

* Outcome 3: Hospital admission rate: $\text{Hospital admission rate} = \frac{\text{Total number of admissions per follow-up period}}{\text{Total follow-up year per person per follow-up period}}$

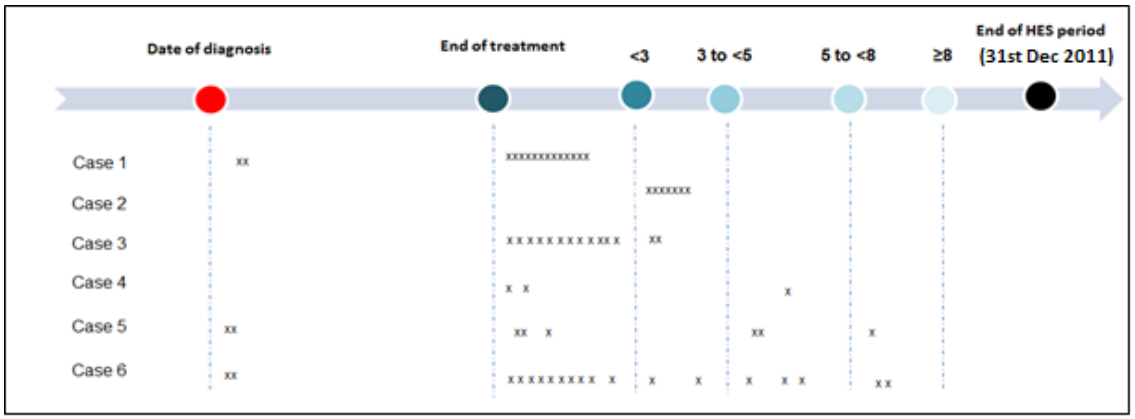


Figure 18: Example 2: hospital inpatient admissions on a time scale diagram

The pattern of hospital admissions was analysed by year of admission (1997-2011). This was done to examine the general pattern of admissions across the study period, and to check whether the pattern altered after 2005 when the NHS produced guidance to improve young people's outcomes by introducing age-appropriate specialist centres to ensure that centralised care was delivered equitably (see Chapter 2, Section 2.4).

A univariable analysis was carried out to compare the pattern of the median rates of admission/admission duration, separately by age at diagnosis, sex, ethnicity, deprivation and relapse status for all cancers combined and by major histological sub-types. The difference of distribution of the rate of admissions/length of stay between age groups and cancer types was tested by different statistical tests depending on the distribution of the study variables: outcome or the dependent variable (the rate of admissions and length of stay) and the independent variables (age group and cancer type). *t*-test was used for normally distributed continuous outcome (dependent) variables and the Mann-Whitney U-test for testing the distribution of continuous non-normally distribute outcome variable and two independent variable. Kruskal–Wallis was also used when comparing between more than two independent group and non-normally distributed dependent variable. This was done to assess whether the hospital burden was significantly varied by age group and cancer types in each admission phase.

The median number of admissions was calculated for each individual per one person-years from date of diagnosis until the end of the follow-up period, including in treatment and post treatment phases, while the duration of each admission was estimated per 100 bed-days per person.

4.12.3 Hospital admission rate ratio and day rate ratio

Rates of hospital admissions could be higher within the first year after diagnosis and is believed to follow a Poisson distribution (albeit, positively skewed) [72].

In order to model the hospital admission rate ratio (HRR) and number of days in hospital rate ratio (DRR), a Poisson model using the total number of admissions/number of days for cancer patients as an outcome variable, adjusting for person-years/person-days as an exposure, was fitted to the data. The model fit was checked using two tests: the estat gof [193] command in Stata based upon the Chi-squared test, while the second test assessed the distribution of the observations using scatter plots, and any violation of the Poisson assumption would be determined if the mean of the distribution was not equal to the variance, inferring that negative binomial regression would be better implemented instead [194, 195].

After choosing the most appropriate model distribution, a model building process was conducted to determine which variables should be included in the final model for each diagnostic group. To determine this choice, the Bayesian information criterion (BIC) was chosen rather than Akaike's information criterion [196]. There is evidence that the BIC is a more consistent approach in selecting the best-fitting model compared to AIC [197, 198]. The choice of independent variables included in the models was based primarily on clinical importance and the variable type (categorical vs. continuous) was based on statistical importance. The BIC compares the probability that each assessed model is the true model in estimating the observed data (such as the mean of the outcome). Additionally, there is a natural penalty for including a larger number of independent variables, hence more emphasis on parsimonious models [198]. Furthermore, the number of cases within the main diagnostic groups could limit the study power, therefore BIC was felt to be a more appropriate choice than AIC, as it focuses on the least complex model that explains most of the variation in the data.

A strength of the modelling approach was the ability to adjust for case mix when assessing rates of hospital admissions or length of stay. Casemix characteristics included: gender, age at diagnosis (continuous, categorical (children and TYA), or four-year age bands (0-4, 5-9, 10-14, 15-19, 20-24, 25-29), year of diagnosis (categorical or continuous), ethnicity (South Asian vs non-South Asian), deprivation (Townsend score, continuous or categorical), proportion of specialist care admissions/specialist care days (continuous or categorical), ever relapsed (yes vs. no) and type of initial treatment (chemotherapy alone, radiotherapy alone, surgery alone, chemotherapy and radiotherapy, chemotherapy and surgery, radiotherapy and surgery, combination of all three modalities, no recorded treatment). These variables were chosen based on their potential impact in explaining variation in levels of hospitalisation, as identified in the literature in addition to clinical input (as described in Chapter 3).

Several sensitivity analyses were carried out to assess the impact of including or excluding certain groups from the analysis on the final results. These included the following:

1. Patients who died during the study period compared to those who survived to the end of the study period. This was carried out for all cancers combined. Results are presented in Section 7.2.4. Patients who die may have higher hospital admissions compared with survivors, evident in the deterioration of their health in the period leading up to death.
2. Comparison of the patterns of admission between relapsed and non-relapsed cases. It was hypothesised that those who had relapsed would have more admissions than non-relapsed cases. Results are presented in Section 7.2.3.
3. Patients receiving a BMT vs. those that did not receive a BMT. The differences were assessed comparing leukaemia cases with the other cancer types adjusted for patient clinical and demographic characteristics. This was done to answer clinical concerns, whereby a patient who received a BMT may have more complex clinical needs than those who had not received a BMT.

4.12.4 Causes of hospital admissions

4.12.4.1 Description of morbidity related to hospitalisation

In the HES data, individuals could have several diagnosis contained within a single admission, i.e. a patient could have a primary diagnosis code (the main reason for hospitalisation) and up to 19 additional secondary diagnosis codes (with no particular order of importance). An example of how the data might be arranged is presented in Table 16. The primary code was defined as the main reason for or cause of admission, while secondary causes were any diseases or complications that the individual may have that was suspected to be related to the primary diagnosis. For example: an individual might be admitted for myocardial infarction (MI) and have pre-existing diabetes. The MI would be considered as the main reason for admission and diabetes as the secondary cause of admission.

In HES data, diagnosis of admissions are classified using the International Classification of Disease 10th edition (ICD-10). These codes include alpha numeric codes. In the current analysis, the first three digits were used to group causes into 22 chapter headings. A description of admission codes can be found at: http://digital.nhs.uk/hesdatadictionary.

The number of cases with hospital admissions for all causes combined, and per specific cause of admission, were summarised. Additionally, the primary cause and secondary cause was summarised separately. This was done to check the consistency in coding,

and assess whether using the primary diagnosis might underestimate the impact of certain causes which could often be coded as a secondary diagnosis.

Further analysis was carried out to assess the percentage of admissions for certain primary diagnoses before and after treatment completion for specific cancer types and for all cancers combined. This enabled a description to be made of the contribution of specific causes of admissions for future planning of services. This was performed by dividing the number of admissions occurring before/after the treatment period by the total number of admissions for each cause by cancer type.

Table 16: Example of how causes of admissions were recorded in HES

YCTR_ID	DIAG_01	DIAG_02	DIAG_03	DIAG_04	DIAG_05	DIAG_06	DIAG_07	DIAG_08	DIAG_09	DIAG_10	DIAG_11	DIAG_12	DIAG_13	DIAG_14	DIAG_15	DIAG_16	DIAG_17	DIAG_18	DIAG_19	DIAG_20
XX002	1*	22	10																	
XX002	14	20	3																	
XX002	2	1																		
XX002	8	19	17																	
XX008	7	2	5	18	4	21	21	6	8	14	20	9	17	22	15	3	15	13	11	1
XX008	6																			
XX008	2																			
XX008	4	7	19	17																
XX010	13																			
XX010	11	6																		
XX010	3	4	19	21																
XX011	9	10	12																	
XX011	13																			
XX011	17																			
XX011	18	19	20	5	7	8	11													
XX012	4	3	7																	
XX012	12	17	2	4																

* The causes of admission were recoded into 22 groups using ICD-10 (details of the code definitions are listed in Appendix A).

4.12.4.2 Observed time of admission after completion of cancer treatment

In addition to determining overall hospital burden and the burden of cancer-related morbidity, the time to first hospitalisation after treatment completion was described for all causes and cause-specific admissions. In order to analyse the time to first admission after completion of cancer treatment, time to event (or survival) analysis was used. The date of treatment completion was the study entry date and the exit date was the first date of admission for each specific cause, and censored at date of death, date lost to follow-up or end of study period, whichever occurred first. The time at risk (i.e. the time from treatment completion to hospital admission) was estimated by subtracting the entry date from exit date i.e. the time from study entry until date of occurrence of first event. The median time to hospitalisation and interquartile range was calculated for the total time at risk per main cancer type and age at diagnosis for all causes combined and per specific cause. The difference in time to hospitalisation by cancer type and age group was assessed using the Mann-Whitney U-test [192].

4.12.4.3 Cancer cohort compared with the background population

Data on the general population of admissions was derived from all recorded admissions in HES during the period 1997 to 2011, and matched by age at the time of admission, sex and time period of admission, attributed to individuals who were resident in Yorkshire according to their postal address at the time of admission. The aim of this section was to assess the hospitalisation rate among the cancer cohort compared with all hospitalisations for children and TYA matched according to age, period and sex in the general population.

In order to compare the hospital burden among survivors to the background population, the crude hospitalisation rate of admissions was estimated among the general population using the total number of individuals of the same age, sex and year of admission, with the first admission for a specific cause defined as the outcome variable divided by the annual mid-year age and sex specific population estimate. The total number of people in the population aged between 0 and 45 years was used as the exposure variable. This was used to estimate the expected rate of admission and then indirectly standardise the admission rate ratio for the cancer cohort. Among the cancer cohort, the total number of admissions for certain causes was defined as the outcome variable, while the total follow-up period in years, as explained in Section 4.6.4, was defined as the exposure variable. The standardise hospitalisation rate (SHR) was estimated using indirect standardised hospitalisation rate ratios [199]. This approach allowed estimates to be made of the actual burden of specific causes of admissions among the cancer cohort after completion

of cancer treatment compared to the background population. This approach was similar to other studies that assess the rate of hospitalisation among CYP cancer survival compared with background population [101, 140]. Additionally, it was adopted for comparison purposes, to assess whether the excess rate of hospitalisation among CYP survivors varied by counties. The SHR was further analysed by age at diagnosis, gender and cancer type to identify any sub-group differences. All the analysis was carried out using Stata 14.

The study results were summarised in four chapters to provide a comprehensive analysis of hospital burden among cancer survivors following date of diagnosis. Each chapter is aligned with the study aims and research question, with a description of the study population in Chapter 5, a detailed description of the hospital activity patterns for both the 'on treatment' and 'post treatment' phases in Chapter 6, the multivariable analysis of the factors influencing hospitalisation rates and length of stay in Chapter 7 and a detailed analysis of the cause-specific hospitalisations among cancer patients in Chapter 8.

Chapter 5 Understanding the Study Population

5.1 Introduction

In this thesis, we aimed to identify the healthcare burden among cancer survivors in Yorkshire. This section includes the cancer incidence among cases diagnosed between 1996 and 2009 aged 0-29 years old. Additionally, a comprehensive description of the study populations, including demographic characteristics of age, ethnicity and deprivation, and clinical characteristics such as diagnostic cancer type, type of initial treatment, and proportion of specialist care are provided (Question 1).

This chapter starts by assessing the pattern of cancer incidence by age at diagnosis, gender and the temporal pattern by year of diagnosis, to provide healthcare commissioners with an updated record of the pattern of cancer incidence. Additionally, to cross-check if the study population resembles the national incidence pattern and highlight the potential to extend the study result to the national level. The second part contains a sensitivity analysis to compare the distribution of linked cases with cases with no linked hospital record, by analysing the distributions of age, sex, ethnicity and deprivation among the cancer cohort. The last part in this chapter provides a descriptive analysis of the study population's clinical characteristics, including distribution of type of initial treatment, BMT, relapse of disease and proportions of specialist care by cancer types.

5.2 Methods

Case information was extracted from the YSRCCYP to identify CYP cancer survivors before their 30th birthday and diagnosed between 1st January 1996 and 31st December 2009 and living in Yorkshire when diagnosed. These were linked to hospital admissions extracted from HES from 1st April 1997 until 31st December 2011, using NHS number, date of birth, gender and postcode when diagnosed. The linkage method was the same for both inpatient and outpatient admissions (for more detail see Section 4.7).

The cancer incidence rate was calculated using age and sex standardised incidence rates, using single mid-year population estimates as person-years (more detail in Chapter 4).

The differences between linked and non-linked cases were compared using chi-square tests for categorical data. The comparison was done for age group at diagnosis (0-14 or 15-29 years), gender, period of diagnosis, cancer type (ICCC-3), deprivation using Townsend quintile [200] and ethnicity (South Asian or non-South Asian).

5.3 Results

5.3.1 Cancer incidence

Leukaemia was the commonest diagnostic group among children aged 0-14 at diagnosis in both genders, with male and female incidence rates of 11.0 and 10.0 per million person-years, respectively. Among TYAs, germ cell tumours were the commonest diagnostic group for males (ASR=25.0; 95%CI 22.0-27.0 per million people). While, the commonest diagnostic group among females was lymphoma (ASR=12.0; 95% CI10.0-13.0 per million people) (Table 17). There was a higher male cancer incidence compared with females (ASR=101.0 and 68.0 per million people, respectively).

Overall, cancer incidence was higher among TYAs than children. The rate of incidence fluctuated based on the year of diagnosis, among children it peaked in 2002 (ASR=165 per million people; 95%CI 135-195) and among TYAs peaked around 2005 (ASR=265 per million people; 95%CI 228-301) (Figure 20).

Table 17: Distribution of cancer incidence per million people by age group, gender and diagnostic group (ICCC3)

Cancer diagnostic Group (ICCC-3)	Children (0-14 years)				TYAs (15-29 years)				Total (0-29 years)					
	Male		Female		Male		Female		Male		Female		Total	
	ASR*	95% CI¥	ASR	95%CI	ASR	95%CI	ASR	95%CI	ASR	95% CI	ASR	95% CI	ASR	95% CI
Leukaemia	11.0	(10.0-12.0)	10.0	(8.0-11.0)	6.0	(5.0-7.0)	5.0	(4.0-6.0)	17.0	(15.0-19.0)	15.0	(13.0-16.0)	31.0	(29.0-34.0)
Lymphoma	5.0	(4.0-6.0)	3.0	(2.0-4.0)	14.0	(13.0-16.0)	12.0	(10.0-13.0)	19.0	(17.0-21.0)	14.0	(13.0-16.0)	33.0	(31.0-36.0)
CNS	8.0	(7.0-8.0)	6.0	(5.0-7.0)	7.0	(6.0-8.0)	6.0	(5.0-7.0)	15.0	(13.0-16.0)	13.0	(11.0-14.0)	27.0	(25.0-29.0)
Neuroblastoma	3.0	(2.0-3.0)	2.0	(1.0-3.0)	0.0	(0.0-1.0)	0.0	(0.0-0.0)	3.0	(2.0-4.0)	2.0	(2.0-3.0)	5.0	(4.0-6.0)
Retinoblastoma	1.0	(1.0-1.0)	1.0	(0.0-1.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	1.0	(1.0-1.0)	1.0	(0.0-1.0)	2.0	(1.0-2.0)
Renal tumours	2.0	(2.0-3.0)	2.0	(1.0-2.0)	1.0	(0.0-1.0)	1.0	(0.0-1.0)	3.0	(2.0-4.0)	2.0	(2.0-3.0)	5.0	(4.0-6.0)
Hepatic tumours	0.0	(0.0-1.0)	0.0	(0.0-1.0)	1.0	(0.0-1.0)	0.0	(0.0-0.0)	1.0	(0.0-1.0)	1.0	(0.0-1.0)	2.0	(1.0-2.0)
Bone tumours	2.0	(1.0-2.0)	1.0	(1.0-1.0)	3.0	(2.0-4.0)	2.0	(1.0-3.0)	5.0	(4.0-6.0)	3.0	(2.0-4.0)	8.0	(7.0-9.0)
STS	3.0	(3.0-4.0)	2.0	(1.0-3.0)	4.0	(3.0-5.0)	4.0	(3.0-5.0)	8.0	(6.0-9.0)	6.0	(5.0-7.0)	13.0	(12.0-15.0)
Germ cell tumours	2.0	(1.0-2.0)	2.0	(1.0-2.0)	25.0	(22.0-27.0)	3.0	(2.0-3.0)	26.0	(24.0-29.0)	4.0	(3.0-5.0)	31.0	(28.0-33.0)
Other epithelial tumours	1.0	(0.0-1.0)	1.0	(0.0-1.0)	3.0	(2.0-4.0)	7.0	(6.0-8.0)	4.0	(3.0-5.0)	7.0	(6.0-9.0)	11.0	(10.0-13.0)
Other unspecified tumours	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-0.0)	0.0	(0.0-1.0)	1.0	(0.0-1.0)
Total cancers	38.0	(35.0-40.0)	29.0	(27.0-32.0)	64.0	(60.0-67.0)	39.0	(36.0-42.0)	101.0	(97.0-106.0)	68.0	(65.0-72.0)	170.0	(164.0-175.0)

Abbreviations: ASR - age and sex standardise incidence rates; CI - confidence interval; CNS - central nervous system; STS - soft tissue sarcoma

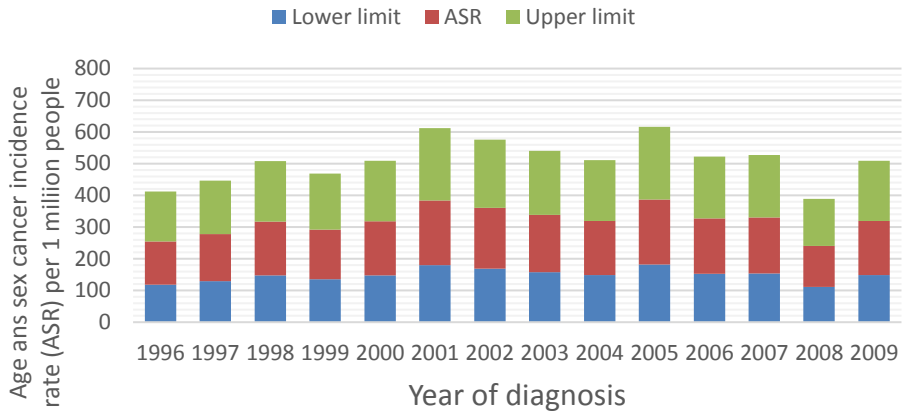


Figure 19: Age and sex standardise incidence rate per million people by year of diagnosis for cases aged 0-29 years at diagnosis

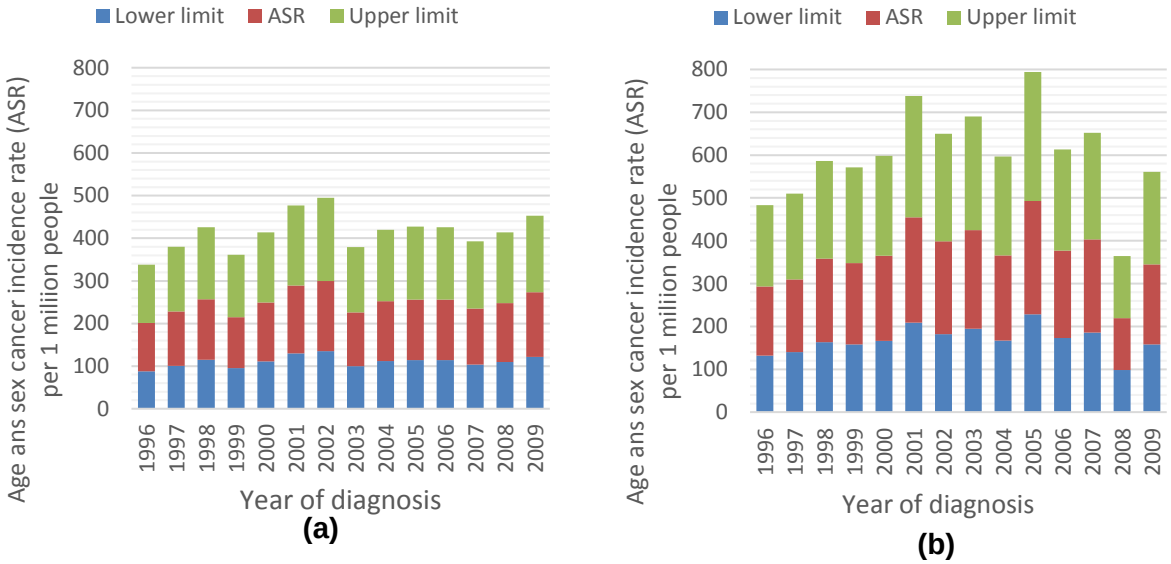


Figure 20: Age and sex standardise incidence rate per million people by year at diagnosis for cases aged 0-14 years (a) and 15-29 years (b)

5.3.2 Sensitivity analysis of the distribution of linked and non-linked cases

There were 3,437 cases diagnosed with cancer between 1996 and 2009 aged 0-29 years in Yorkshire. Of those, 3,315 (96.2%) cases were successfully linked to at least one hospital record. After excluding cases that were only admitted before diagnosis, 3,151 (95%) cases were eligible for analysis.

The demographic and clinical characteristics of linked compared with non-linked cases is illustrated in Table 18. There were no statistical differences between the distribution of linked and non-linked cases in terms of gender, diagnostic group and deprivation. However, the distribution of cases by age at diagnosis, period of diagnosis and ethnicity were found to be statistically different. In both groups, there were disproportionately more

TYA cases than children, and more males than females. The majority of non-linked cases were diagnosed early in 1996 to 1999, this could indicate that the documentation of HES during that period was not as good as documentation in 2000-2004 and 2009-2010 when the payment by result started (more detail in Section 4.6.2).

Table 18: Differences in patient characteristics between linked and non-linked cases with hospital episode statistic data

Patient characteristics	Non-linked		Linked		Total		Test statistic (Chi^2)	P-value
	N	%	N	%	N	%		
Age at diagnosis								
0-14	21	17%	1,336	40%	1,357	39%	26.25	<0.001
15-29	101	83%	1,979	60%	2,080	61%		
Gender								
Male	83	68%	1,968	59%	2,051	60%	3.76	0.055
Female	39	32%	1,347	41%	1,386	40%		
Period of diagnosis								
1996-1999	67	55%	807	24%	874	25%	70.4	<0.001
2000-2004	11	9%	1,270	38%	1,281	37%		
2005-2009	44	36%	1,238	37%	1,282	37%		
Diagnostic group ICCC-3								
Leukaemia	14	11%	624	19%	638	19%	18.5	0.07
Lymphoma	31	25%	647	20%	678	20%		
CNS	22	18%	528	16%	550	16%		
Neuroblastoma	<5	1%	#	3%	104	3%		
Retinoblastoma	<5	3%	#	1%	38	1%		
Renal tumours	<5	3%	#	3%	103	3%		
Hepatic tumours	<5	1%	#	1%	32	1%		
Bone tumours	<5	2%	#	5%	155	5%		
STS	7	6%	266	8%	273	8%		
Germ cell tumours	24	20%	600	18%	624	18%		
Other epithelial tumours	11	9%	220	7%	231	7%		
Other unspecified tumours	<5	1%	#	0%	11	0%		
Ethnicity¥								
Non-South Asian	115	94%	3,006	91%	3,121	91%	29.8	<0.001
South Asian	6	5%	309	9%	315	9%		
Unknown	<5	1%	0	0%	<5	0%		
Deprivation*								
Least deprived	25	20%	564	17%	589	17%	8.58	0.072
2	31	25%	609	18%	640	19%		
3	19	16%	632	19%	651	19%		
4	13	11%	608	18%	621	18%		
Most deprived	34	28%	902	27%	936	27%		
Total	122	100%	3,315	100%	3,437	100%		

¥ The classifications of ethnicity were assigned using a combination of cancer register, HES data and name recognition software (SANGARA and Onomap)

*Townsend score

used to prevent disclosure of counts <5

5.3.3 Study population

5.3.3.1 Linked cases: clinical characteristics

For the following section, the results focus on cases with linked admissions, using only the main cancer diagnostic group. The number of cases were summarised by diagnostic group and patient characteristics: age at diagnosis, gender, ethnicity, deprivation and relapse status (Table 19).

There were more TYA than children diagnosed with lymphoma, bone tumours, STS and germ cell tumours, whilst there were more children diagnosed with neuroblastoma and renal tumours. Overall, there were more male cases than females and most of them were of non-South Asian ethnic origin. The percentage of cases increased with an increased level of deprivation. 14% of cases relapsed at least once, and the number of relapsed patients was highest among cases diagnosed with bone tumours.

Table 19: Distribution of number of cases by diagnostic group and demographic characteristics

Patient characteristics	Leukaemia		Lymphoma		CNS		Neuroblastoma		Renal tumours		Bone tumours		STS		Germ cell tumours		Overall cancers	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Age at diagnosis																		
0-14	408	66.3	149	23.5	257	55.5	87	90.6	76	82.6	53	35.3	107	42.5	65	11.5	1,202	41.9
15-29	207	33.7	486	76.5	206	44.5	9	9.4	16	17.4	97	64.7	145	57.5	499	88.5	1,665	58.1
Gender																		
Male	328	53.3	358	56.4	248	53.6	56	58.3	51	55.4	92	61.3	140	55.6	486	86.2	1,759	61.4
Female	287	46.7	277	43.6	215	46.4	40	41.7	41	44.6	58	38.7	112	44.4	78	13.8	1,108	38.6
Ethnicity																		
Non-South Asian	558	90.7	566	89.1	429	92.7	90	93.8	84	91.3	141	94.0	227	90.1	525	93.1	2,620	91.4
South Asian	57	9.3	69	10.9	34	7.3	6	6.3	8	8.7	9	6.0	25	9.9	39	6.9	247	8.6
Deprivation score																		
Least deprived	110	17.9	121	19.1	83	17.9	20	20.8	14	15.2	24	16.0	36	14.3	93	16.5	501	17.5
2	114	18.5	111	17.5	96	20.7	25	26.0	15	16.3	27	18.0	41	16.3	110	19.5	539	18.8
3	123	20.0	117	18.4	82	17.7	12	12.5	13	14.1	34	22.7	49	19.4	118	20.9	548	19.1
4	98	15.9	114	18.0	85	18.4	17	17.7	23	25.0	27	18.0	49	19.4	102	18.1	515	18.0
Most deprived	170	27.6	172	27.1	117	25.3	22	22.9	27	29.3	38	25.3	77	30.6	141	25.0	764	26.6
Relapsed																		
No	515	83.7	555	87.4	396	85.5	75	78.1	82	89.1	112	74.7	206	81.7	531	94.1	2,472	86.2
Yes	100	16.3	80	12.6	67	14.5	21	21.9	10	10.9	38	25.3	46	18.3	33	5.9	395	13.8
Total	615	100.0	635	100.0	463	100.0	96	100.0	92	100.0	150	100.0	252	100.0	564	100.0	2,867	100.0

Abbreviations: CNS = central nervous system; STS= soft tissue sarcoma; *Townsend deprivation index

5.3.3.2 Initial treatment

Using the cancer register, 14% (375) of cases had no recorded details of any treatment having been received at or near the time of diagnosis. The HES data were used to cross-check the type of treatment received using procedure codes, especially among those cases for which there was no recorded treatment. Details on identifying initial treatment and the data sources can be found in Section 4.11.3

Recording of treatment was poor in HES compared with the cancer register, especially for radiotherapy, where the percentage of completeness was 5%, and major surgery was 19% (Table 20). While, the percentage of treatment completeness in the cancer register was high, ranging from 85% to 97% (Table 20 and Table 21).

Cases with no record of treatment in the cancer register (n= 375) were validated using medical notes (detail in Section 4.11.4.1), and a third (~70%) of those cases were cases with no actual recorded treatment.

Table 20: Number of cases recorded and percentage of completeness by type of initial treatment identified by HES

Type of initial treatment	HES		Total number of cases from all sources*	
	N	%	N	%
Chemotherapy	1,552	75	2,060	100
Radiotherapy	25	5	513	100
Surgery	233	19	1,226	100

Abbreviations: N =number of cases with the recorded treatment; %= percentage of completeness; *Identification of treatment using cancer register, HES and internal inspection through cases medical notes.

Table 21: Number of cases recorded and percentage of completeness by type of initial treatment identified by cancer register

Type of initial treatment	Cancer register		Total number of cases from all sources*	
	N	%	N	%
Chemotherapy	1,875	91	2,060	100
Radiotherapy	499	97	513	100
Surgery	1,042	85	1,226	100

Abbreviations: N = number of cases with the recorded treatment; % = percentage of completeness; *Identification of treatment using cancer register, HES and internal inspection through cases medical notes.

There was no formal field recording the date of treatment completion on the cancer register. A matrix was therefore created to identify the approximate date of completion of treatment. This method was described in detail in Section 4.11.4.2. The result of this

matrix found that, overall, chemotherapy alone, followed by chemotherapy and surgery, were the most common treatment modalities, followed by surgery alone (Table 23), with only 7% of cases having no recorded treatment. CNS tumours had the highest percentage of no recorded treatment. Possible reasons for having no recorded treatment could include death before the start of treatment, or minor surgical procedures (i.e. not considered to be curative treatment), or they may have truly not been treated.

Based on the third Improving Outcomes Strategy report [9], it was recommended that cases diagnosed with cancer should not wait more than 31 days to receive their initial treatment to ensure optimal treatment is received equally [9]. However, the time to first initial treatment varied by age group and diagnostic group in the current analysis (Table 22). Overall, the median time to initial treatment was within a month of diagnosis (median 22, IQR=2-67), it was shorter among children than TYAs, where the medians were 0 and 35 days, respectively.

Table 22: Number of cases and median and inter-quartile range of total number of days until initial treatment from date of diagnosis

Cancer type	0-14			15-29			0-29		
	N	Median	IQR	N	Median	IQR	N	Median	IQR
Leukaemia	399	1	0 - 3	197	7	2 - 64	596	2	1- 11
Lymphoma	146	10	5 - 23	469	31	17-118	615	25	11- 68
CNS	206	34	0 -103	159	49	0-139	365	38	0-122
Neuroblastoma	80	7	1 -126	7	104	33-180	87	7	1-131
Renal tumours	76	7	1 - 41	16	0	0-1,133	92	6	0-41
Bone tumours	51	27	12-166	92	89.5	89-207	143	64	18-198
STS	98	21	4-116	131	29	0-151	229	24	0-130
Germ cell tumours	58	0	0-35	494	35	12-58	552	34	5- 57
Overall cancers*	1,114	5	1-38	1,565	33	8-93	2,679	22	2- 67

Abbreviations:
STS = soft tissue sarcoma
N = number of cases
IQR = interquartile range
* Overall cancers is a total of cases with main cancer type with known treatment

Table 23: Distribution of number and percentage of cases by type of initial treatment and diagnostic group using International Classification of Childhood Cancer (ICCC-3)

Diagnostic group ICCC-3	**Leukaemia**		**Lymphoma**		**CNS**		**Neuroblastoma**		**Renal tumours**		**Bone tumours**		**STS**		**Germ cell tumours**		**Overall cancers**	
	N	%	**N**	%	**N**	%	**N**	%	**N**	%	**N**	%	**N**	%	**N**	%	**N**	%
Chemotherapy alone	528	86	399	63	47	10	26	27	29	32	56	37	55	22	40	7	1,180	41
Radiotherapy alone	<5	0	24	4	27	6	0	0	0	0	<5	1	<5	2	<5	0	62	2
Surgery alone*	<5	0	#	2	133	29	24	25	22	24	19	13	76	30	130	23	417	15
Chemotherapy and radiotherapy	47	8	78	12	34	7	5	5	<5	2	8	5	36	14	#	1	215	7
Chemotherapy and surgery	14	2	75	12	45	10	27	28	35	38	52	35	42	17	278	49	568	20
Radiotherapy and surgery	<5	0	11	2	31	7	<5	1	0	0	<5	1	#	2	89	16	139	5
Chemotherapy, radiotherapy and surgery	<5	0	16	3	48	10	<5	4	<5	4	<5	3	11	4	8	1	97	3
No recorded treatment	20	3	20	3	98	21	9	9	0	0	#	5	23	9	12	2	189	7
Total¥	615	100	635	100	463	100	96	100	92	100	150	100	252	100	564	100	2,867	100

*Only cancer related major surgeries, detail of surgery code is included in the appendices.

¥ includes cases with minor surgeries, cases that died before treatment started, no record of treatment.

figures removed to avoid disclosure of potentially identifiable data.

5.3.3.3 Patients with bone marrow transplant (BMT)

One of the essential variables for estimating the date of treatment completion was if a patient received a BMT, and when it had been received (as described in Section 4.11.4.2).

BMT was identified using the cancer register procedure code and the HES inpatient records (defined in Section 4.11.4.4). For further assurance, a list of patients having BMTs were provided from one of the principle treatment centres responsible for the majority of BMTs in Yorkshire, and cross-checked with the list of study cases. The cancer register identified only 7% of BMTs (12 out of 168), while HES identified 47% of BMTs (79 out of 168 total cases in the provided list). This was evidence of poor documentation of BMTs in the study data sources, where a total of 84 (53%) were not identified using either of the study sources.

In total almost 6% (n=168) of cases had BMTs during the course of their treatment. Neuroblastoma cases had the highest percentage of BMT, followed by leukaemia cases, having 25% and 15%, respectively out of the total number of cancer cases (Table 24).

Table 24: Distribution of cases with BMT by main cancer diagnostic group

Diagnostic group	Number of cases with BMT	Percentage	Total number of cases
Leukaemia	95	15.4%	615
Lymphoma	31	4.9%	635
CNS	<5	<1%	463
Neuroblastoma	24	25.0%	96
Renal tumours	<5	<2%	92
Bone tumours	8	5.3%	150
STS	7	2.8%	252
Germ cells tumours	0	0.0%	564
Overall cancers	168	5.9%	2,867

5.3.3.4 Relapsed cases

Another important variable that could affect the estimation of treatment completion was patient relapse. Detail on the definition and source is in Section 4.11.4.3. There were 14% (n=395) of cases with a recorded relapse (Table 25)of which 23% (n=92) had multiple relapses. Bone tumours, neuroblastoma, STS and leukaemia had the highest percentage of relapses having 25%, 22%,18% and 16%, respectively (Table 25) 21% (n= 86) of relapsed cases had a BMT, and of those 65% (n=56) had a BMT after relapse.

Table 25: Distribution of number of cases by number of relapses

Cancer group ICCC-3	Number of relapses						Total number of cases
	1		⩾2		Total relapses		
	N	%	N	%	N	%	N
Leukaemia	81	81%	19	19%	100	16%	615
Lymphoma	51	64%	29	36%	80	13%	635
CNS	56	84%	11	16%	67	14%	463
Neuroblastoma	16	76%	5	24%	21	22%	96
Renal tumours	#	70%	<5	30%	#	11%	92
Bone tumours	24	63%	14	37%	38	25%	150
STS	38	83%	8	17%	46	18%	252
Germ cell tumours	#	91%	<5	9%	#	6%	564
Overall cancers	303	77%	92	23%	395	14%	2,867

Abbreviation: ICCC-3 = International Classifications of Childhood Cancer; N = number of cases; CNS = central nervous system; STS = soft tissue sarcoma.
figures removed to avoid disclosure of potentially identifiable data

5.3.3.5 Proportion of specialist care

The place of care was extracted from cancer register to identify place of care when diagnosed, and from HES to identify place of care when admitted. The documentation of place of care in the cancer register was not complete as 40% of total cases had unknown hospital names when diagnosed. This could be due to patients being diagnosed abroad or their place of care not being documented in the cancer register. While in HES, the place of care when admitted was complete. Therefore, survivors were allocated to specific place of care – specialist or other non-specialist – using HES records. The healthcare providers at admission were considered as specialist if they were one of the childhood specialist oncology centres, principle treatment centres or tumour specific centres; a list of these centres was documented in Section 4.11.6.

The place of care during admission was classified as to specialist healthcare setting or other non-specialist NHS healthcare setting, giving the hospital name and address as described in Section 4.11.6.

The use of hospital care could vary by proportion of specialist care, thus it was important to assess the distribution of cases by the proportion of specialist care, before including them in the multivariable model. The proportion of specialist care was estimated in two different ways, depending on the study outcome: number of admissions or number of days. For the number of admissions, the number of specialist admissions during the study period was used, and when the number of days was the outcome in the multivariable analysis, the number of days spent in specialist admissions was used. (These were described earlier in Section 4.11.6.) The variations in hospital activity giving

the proportions of specialist care were compared by age group and cancer type for both groups using the proportion of specialist admissions and proportion of specialist stays.

For all cases, the proportion of specialist care varied by cancer type and ranged from 33% to 78% of total admissions. Cases with neuroblastoma had the highest percentage of ‘mostly specialist’ care, followed by bone tumours and leukaemia, where the percentages were 78%, 72% and 72%, respectively. ‘Other malignant epithelial tumours’ and ‘other and unspecified malignant neoplasms’ had the lowest percentage of ‘mostly specialist’ care (Figure 21).

Children were likely to have higher specialist admissions than TYAs, having 74% and 40% for children and TYA, respectively (Figure 22). This could indicate the availability of specialist hospitals for each age group. The study survivors population lived in Yorkshire during diagnosis, therefore the majority were admitted to Leeds General Infirmary, St James's University Hospital, or Sheffield Children's Hospital, having 41%, 49% and 7%, respectively, of all admissions to specialist units for survivors aged 0-29 years at diagnosis. However, the proportion varied by age group. Children aged up to 14 were commonly admitted to St James's University Hospital, followed by Leeds General Infirmary with 51% and 38%, respectively, while TYAs aged 15-29 were admitted to Leeds General Infirmary more regularly than St James's University Hospital with 49% and 45%, respectively (Figure 23). Children admitted to Sheffield Children's Hospital made up 9% of total admissions to a specialist unit, while this figure was only 1% for survivors aged 15-29 years. TYAs were more likely to be admitted to centres outside the Yorkshire boundary than children, as 2% of admissions to specialist units were for Newcastle Upon Tyne Hospitals including, the Freeman Hospital, Weston Park Hospital and the Royal Victoria Infirmary, compared with only 1% among children (Figure 23). Similarly, the percentage of admissions among TYAs was higher than children for the Royal Victoria Infirmary, and University Hospitals in Bristol.

Among children, cases with leukaemia and lymphoma had the highest ‘mostly specialist admissions’ compared to other cancer types. Among TYAs, bone tumour survivors had highest ‘mostly specialist admissions’. The proportion of specialist stays were similar to the proportion of specialist admissions by diagnostic group and age group.

The number of cases with no specialist care during the follow-up period, were mainly aged 20-24 and 25-29 years at diagnosis with 27% (n=228) and 46% (n=394) of the total number of cases having no specialist admissions, respectively. While this figure was less than 15% among cases diagnosed under 15 years of age.

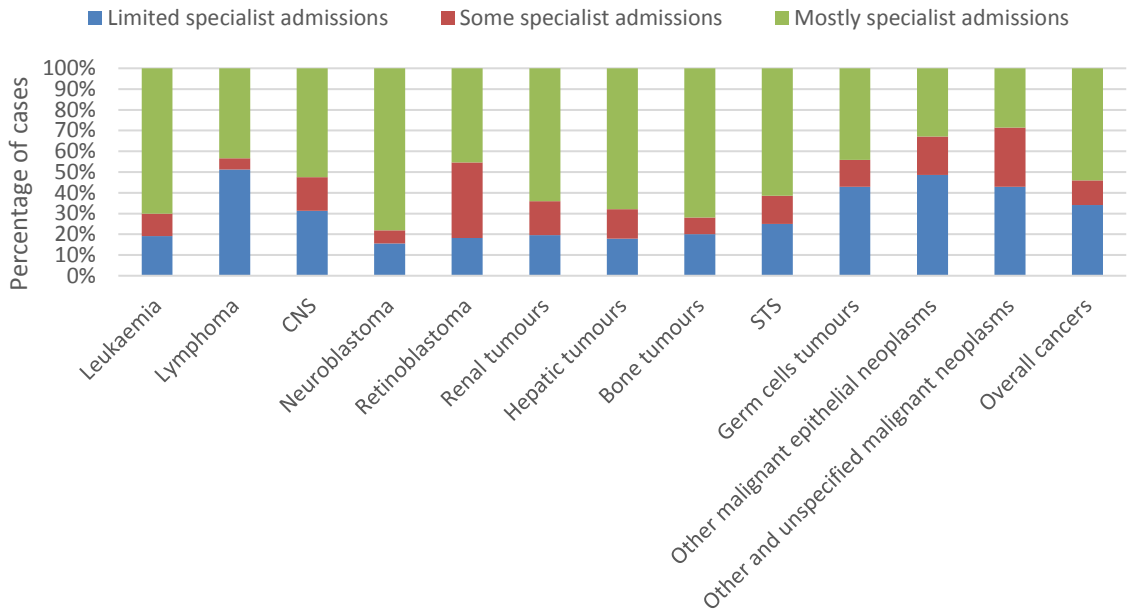


Figure 21: Percentage of cases by proportion of specialist admissions for cases aged 0-29 years and cancer types ICCC-3

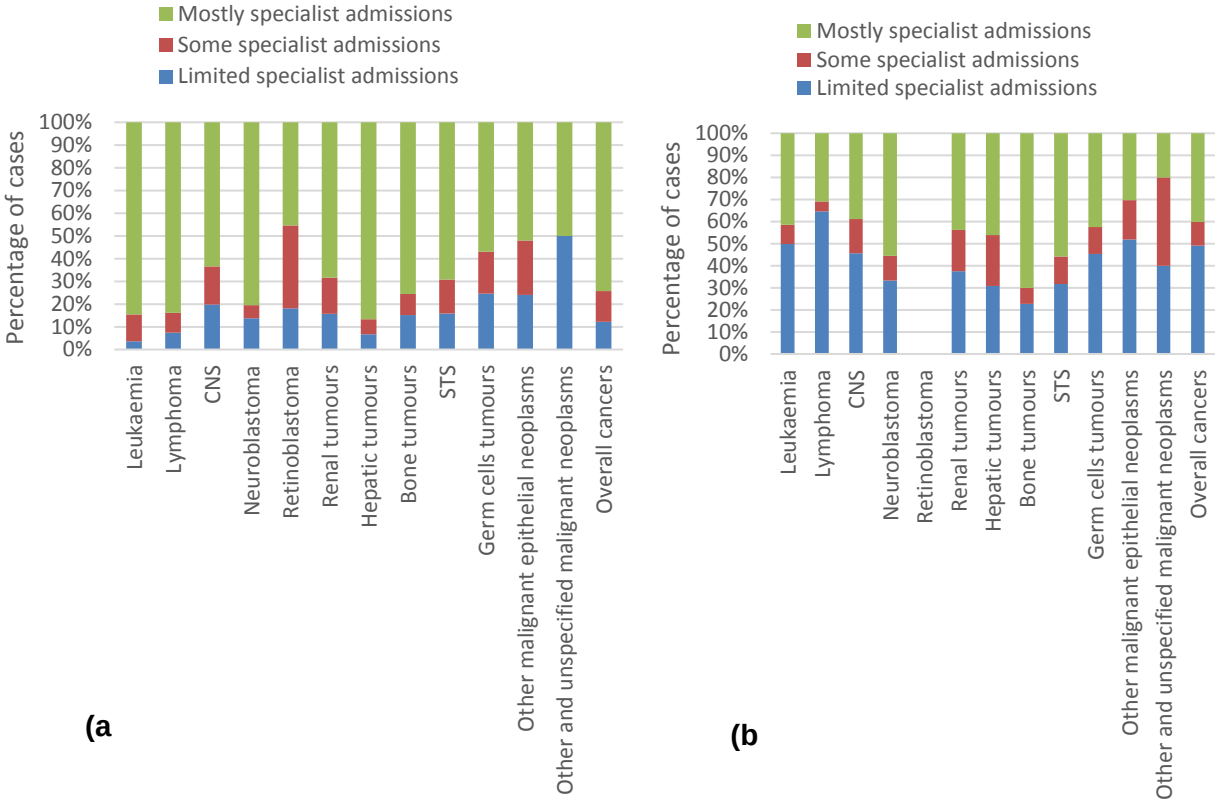


Figure 22: Percentage of cases by proportion of specialist admissions for (a) children and (b) TYAs by cancer types ICCC-3

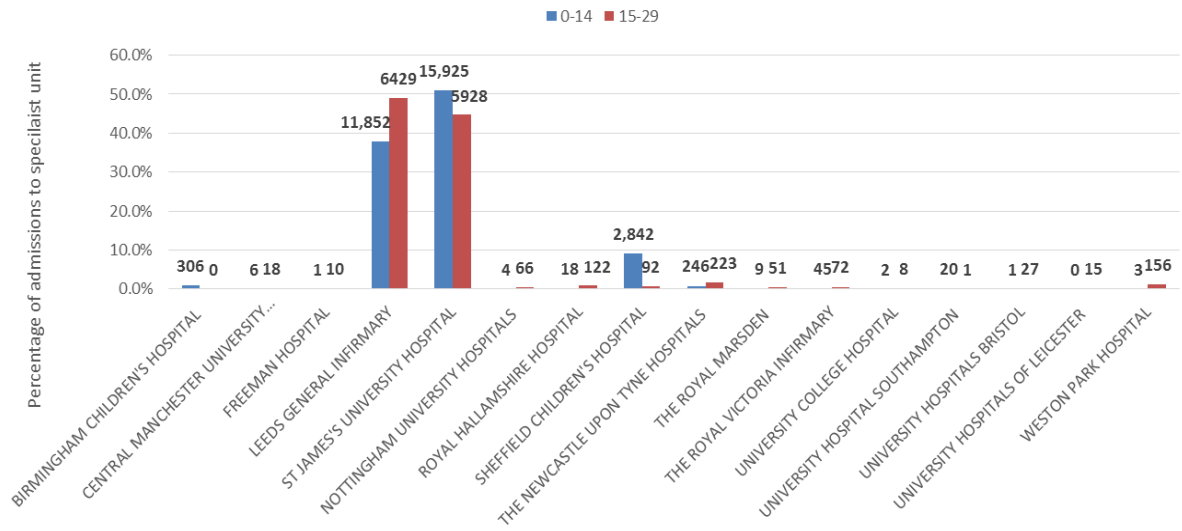


Figure 23: Percentage of admissions to specialist unit by hospital names and age group

5.4 Summary

Children, teenagers and young adults are the focus of this thesis, although the cancer incidence is rare among this age group, less than 1% for children aged up to 24 and around 10% among the 24-39 years of age population [36]. However, cancer has fatal effects among this age group, in addition to long-term disabilities and years lost in hospital [147]. Cancer incidence among the former area of Yorkshire resembles the England national average cancer incidence during 2011 to 2013 [75]. Additionally, the pattern of incidence by gender resembled the 2011 distribution of cancer incidence by gender in the UK, where cancers were more common among males than females aged 0-29 at diagnosis. The incidence rate increased by age in England [75], which reflects the higher rate of cancer incidence among TYAs than children.

Among the study population, leukaemia cases were the most common diagnostic group among children, followed by CNS tumours. Among TYAs the commonest diagnostic group was germ cell tumours among males and lymphomas among females, this pattern was similar to the UK incidence pattern [39].

The incidence of cancer was more common among males than females, and higher in teenagers than children. The rate of cancer incidence peaked in 2002 among children, and in 2005 among TYAs.

Of the figures obtained, 96% were successfully linked records. The rate of linkage improved by time of diagnosis, the number of cases with non-linked records was higher in 1996-1999 than in 2000-2004 and 2005-2009. There were no significant differences

among the distribution of cases, and linked and non-linked cases by main survivor characteristics, such as gender, deprivation and type of cancer.

Overall, chemotherapy alone, followed by chemotherapy and surgery, were the commonest treatment modalities, followed by surgery alone.

Cases diagnosed with neuroblastoma and leukaemia had a higher number of BMTs than other diagnostic groups. Cases with bone tumours, neuroblastomas and leukaemia had higher percentages of relapses than other diagnostic groups.

Finally, 54% of survivors received mostly specialist admission care during the follow-up period, where the percentage varied by cancer type and age. Bone tumours, leukaemia and hepatic tumours saw about 70% of survivors having mostly specialist care, while survivors of ‘other epithelial tumours’ and ‘other unspecified neoplasms’ had about 30% of their admissions in specialist settings. Children were more likely to receive most of their admissions in specialist settings than TYAs, having 74% and 40% of survivors with mostly specialist admissions, respectively.

Chapter 6 Patterns of Hospital Activity

6.1 Introduction

This chapter includes a description of hospital activity (inpatient and outpatient) following the date of diagnosis from 1996 to 2009 (Aim 1). Thus, describing the pattern of inpatient hospital activity post diagnosis of cancer, including hospital activity in the patients' 'on treatment' and 'post treatment' phases. In addition, the variation in the median number of hospital admissions and length of stay by age at diagnosis, gender, ethnicity, deprivation, cancer type and by relapse status are provided (Aim 2, Questions 2 & 3). Furthermore, a detailed assessment of the pattern of hospital admission / length of stay by follow-up period is also presented.

6.2 Inpatient activity

This section covered the following aspects:

I. Assess the distribution of frequency of inpatient hospital admissions during the admission period (1997-2011).
II. Assess the distribution of cases by age group (0-14 and 15-29 years at diagnosis), period of admission (on treatment vs. post-treatment).
III. Assess the distribution of admissions by year and diagnostic group (to check how the frequency of admission varied over follow-up time).
IV. Analyse the median rate of admission per person-years by age at diagnosis, gender, ethnicity and deprivation and follow-up period.
V. Analyse the median rate of number of days spent in hospital per 100 person-days by age at diagnosis and follow-up period).

6.2.1 Hospital admissions

6.2.1.1 Distribution of the number of inpatient admissions

The distribution of the number of admissions during the study period were positively skewed, as the majority of cases had fewer than 100 admissions (complete admission period) (Figure 24) and fewer than 50 admissions per patient during the 'on treatment' or 'post-treatment' phase (Figure 25).

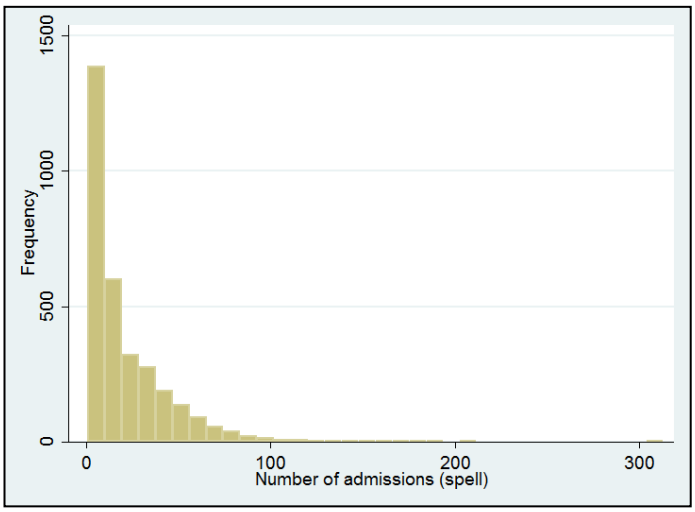


Figure 24: Distribution of hospital admissions per patient post the date of diagnosis

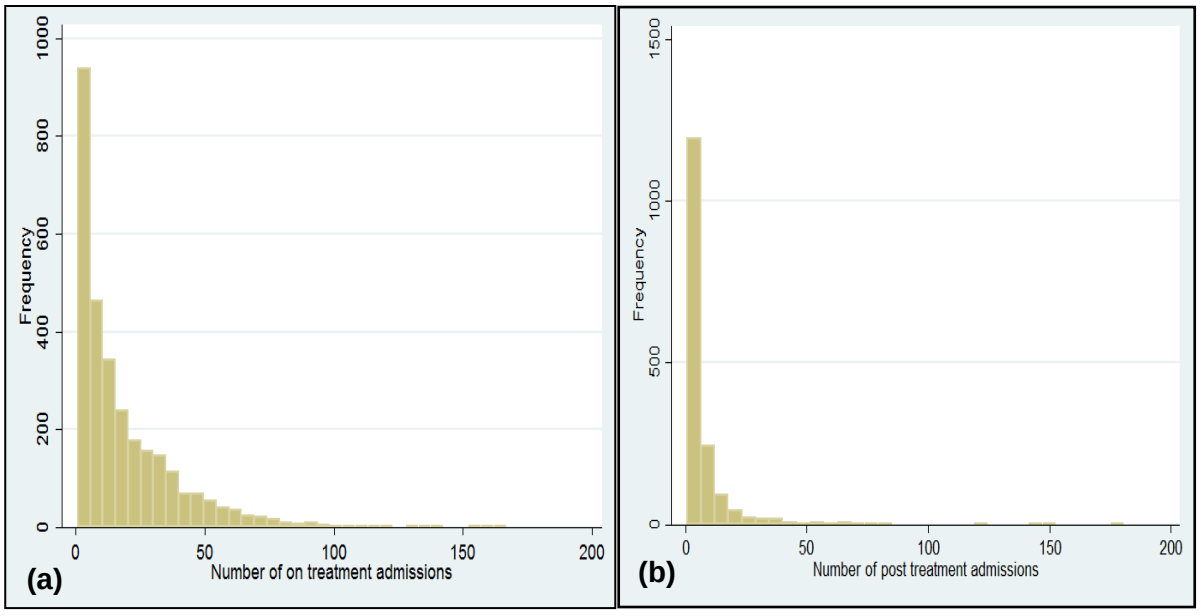


Figure 25: Distribution of hospital admissions per patient during treatment (a) and post-treatment completion (b)

6.2.1.2 Distribution of number of cases by age group and period of admission

There were 61,971 post diagnosis inpatient admissions during the study period 1997-2011 for the main diagnostic groups (leukaemia, lymphoma, CNS, neuroblastoma, renal tumours, bone tumours, STS and germ cell tumours) (Table 26). The majority of inpatient admissions occurred during the treatment period due to treatment purposes or treatment complications. Children had a higher number of admissions than TYAs and there was a significant difference during the treatment period, the interquartile range was 8-38 inpatient admissions and 2-17 admissions for children and TYAs, respectively.

Table 26: Summary table of the number of post diagnosis admissions grouped by period of admission (1997-2011)

	Complete study period			On treatment			Post-treatment		
Age¥	**Total***	**Median**	**Range (IQR)**	**Total**	**Median**	**Range (IQR)**	**Total**	**Median**	**Range (IQR)**
0-14	35,689	25	1-185 (8-44)	30,017	22	1-147 (8-38)	5,672	4	1-152 (2-8)
15-29	26,282	10	1-313 (3-20)	19,814	8	1-167 (2-17)	6,468	3	1-181 (1-7)
0-29	61,971	14	1-313 (5-32)	49,831	12	1-167 (4-28)	12,140	3	1-181 (2-7)

Abbreviations: IQR= Interquartile rage; ¥ Age at diagnosis; *Total is not equal to the sum of on treatment and post-treatment, as it includes the number of admissions for cases with no initial treatment.

The follow-up period from diagnosis until the last admission or censoring ranged from 0-16 years, with a median follow-up per person of seven years. During the treatment period the follow-up period ranged from 1-2 years with a median of one year. During the post-treatment admission period it ranged between1 and 9 years with a median of five years. There was a small difference in the range of follow-up between children and TYAs (Table 27). During the on treatment phase, children were followed-up for two years whilst TYAs were typically followed-up for a year. This could be related to leukaemia patients being followed up for three years from diagnosis whilst completing treatment, whereas TYAs with leukaemia were usually followed-up for two years during treatment.

The rate of admissions was 40 times higher during the treatment period compared to the period after completion of treatment. Children, on average (median), had a higher number of inpatient admissions per person per year during both the on treatment and post-treatment phase, compared to TYAs (1.8 and 1.1 admissions per person per year, respectively) (Table 28).

Table 27: Summary of the number of follow-up years by period of admission

Age	Complete study period			On treatment			Post-treatment		
	Total	Median	Range (IQR)	Total	Median	Range (IQR)	Total	Median	Range (IQR)
0-14	9,195	7	0-16 (3-11)	2,142	1	0-14 (1-2)	7,053	5	0-16 (1-9)
15-29	12,909	6	0-16 (3-10)	2,477	1	0-15 (1-1)	10,431	5	0-16 (1-9)
0-29	22,104	7	0-16 (3-10)	4,620	1	0-15 (1-2)	17,484	5	0-16 (1-9)

Abbreviations: IQR= Interquartile rage; ¥ Age at diagnosis.

Table 28: Summary of admissions per person-years by period of admission and age at diagnosis

Age	Total follow-up Period*			On treatment			Post- treatment		
	Median	Range	IQR	Median	Range	IQR	Median	Range	IQR
0-14	11.5	0.18-1,500	3.51-27.5	42.1	0.7-234.0	23.0-61.0	1.8	0.19-156.8	0.78-4.20
15-29	4.2	0.2-1,000	1.5-13.6	23.0	0.4-1,000	9.4-41.8	1.1	0.2-81.1	0.5-2.4
0-29	6.3	0.2-1,500	2.0-20.0	32.0	0.4-1,000	11.0-50.8	1.3	0.2-156.8	0.6-3.2

Abbreviations: IQR= Interquartile rage; * Follow-up period from date of diagnosis until last admission or censoring.

6.2.1.3 Distribution of number of admissions by year of admission and diagnostic group (ICCC-3)

The periods of admission were grouped into four time periods to facilitate interpretation of the results. There was a slight increase in the percentage of admissions from 2% in 1997 to 6% in 2010 (Figure 26). These admissions were mainly for leukaemia cases having 40% of total admissions (Table 29). The number of inpatient admissions was highest during the 2005-2008 admission periods, having 34% of total admissions (Figure 26).

The hospital admissions were also analysed further by years (1997 to 2011). The rate of admission peaked around 2006, where it reached more than 9% of the total admissions.

During the diagnosis period, incidence rates among children peaked during 2002 and this could explain the first peak in the admission rate (Chapter 5). Additionally, TYAs had the highest incidence rate in 2005 and this could explain the second peak in admission rate in 2005-2008 (Chapter 5).

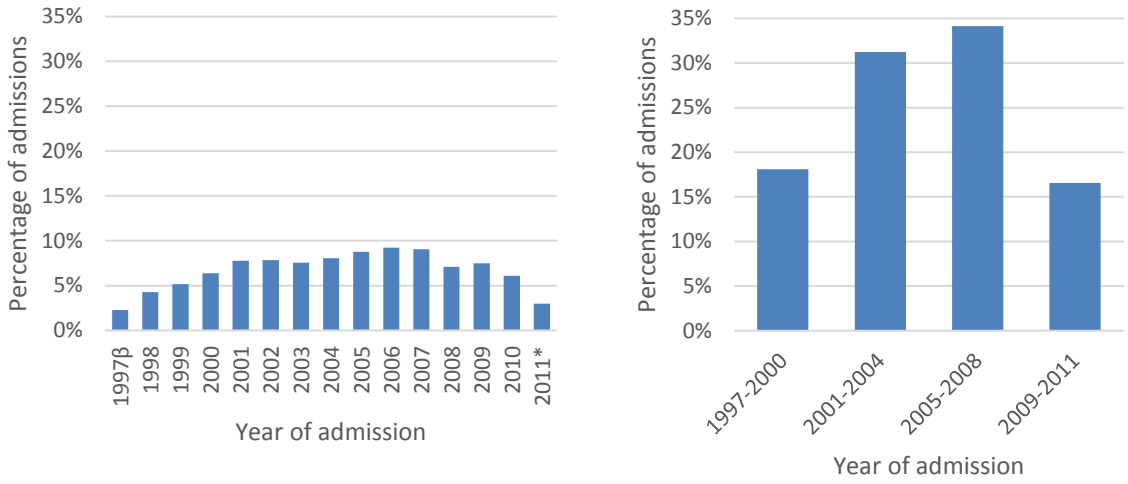


Figure 26: The pattern of inpatient hospital encounters by admission period (1997-2011). Symbols: β Start from 1st of March 1997 (HES annual year); * provisional data may include missing admissions

Table 29: Distributions of number of admissions by year of admission (1997-2011) and diagnostic groups (ICCC-3)

Year of admissions¥	Leukaemia		Lymphoma		CNS		Neuroblastoma		Renal tumours		Bone tumours		STS		Germ cells tumours		Overall admissions	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
1997β	462	33	244	17	142	10	108	8	43	3	159	11	153	11	103	7	1,414	100
1998	1,153	43	489	18	236	9	107	4	68	3	151	6	278	10	172	6	2,654	100
1999	1,331	42	618	19	286	9	113	4	86	3	237	7	377	12	147	5	3,195	100
2000	1,639	42	885	22	360	9	195	5	103	3	198	5	275	7	291	7	3,946	100
2001	1,762	37	1,141	24	592	12	148	3	135	3	394	8	347	7	301	6	4,820	100
2002	1,804	37	1,147	24	548	11	253	5	142	3	294	6	363	7	297	6	4,848	100
2003	1,906	41	1,046	22	490	10	262	6	87	2	296	6	346	7	256	5	4,689	100
2004	2,126	43	1,148	23	593	12	165	3	117	2	281	6	307	6	257	5	4,994	100
2005	2,187	40	1,345	25	583	11	117	2	156	3	327	6	331	6	385	7	5,431	100
2006	2,242	39	1,309	23	615	11	186	3	206	4	380	7	424	7	364	6	5,726	100
2007	2,277	41	1,190	21	540	10	230	4	122	2	418	7	412	7	418	7	5,607	100
2008	1,766	40	889	20	488	11	168	4	124	3	330	8	352	8	266	6	4,383	100
2009	1,613	35	1,050	23	560	12	113	2	124	3	387	8	331	7	463	10	4,641	100
2010	1,546	41	649	17	615	16	146	4	116	3	172	5	323	9	197	5	3,764	100
2011*	688	37	291	16	322	17	109	6	37	2	80	4	167	9	165	9	1,859	100
Total	24,502	40	13,441	22	6,970	11	24,20	4	1,666	3	4,104	7	4,786	8	4,082	7	61,971	100

Symbols: ¥ Calendar annual year (1st of January to 31st December); βStart from 1st of March 1997 (HES annual year); * provisional data may include missing admissions.

The admissions were mainly for cases diagnosed with leukaemia and lymphoma, where around 40% and 20% of the total number of admissions occurred respectively, during the admission period 1997-2011 (Figure 27).

Cases diagnosed with leukaemia accounted for 40% of the total admission in 1997-2000, and in 2009-2011 it decreased to account for 35% of the total admissions. In contrast, CNS, germ cell tumours and other epithelial tumours increased at the end of the admission period from 9% to13%, 6% to 7% and 2% to 5%, respectively.

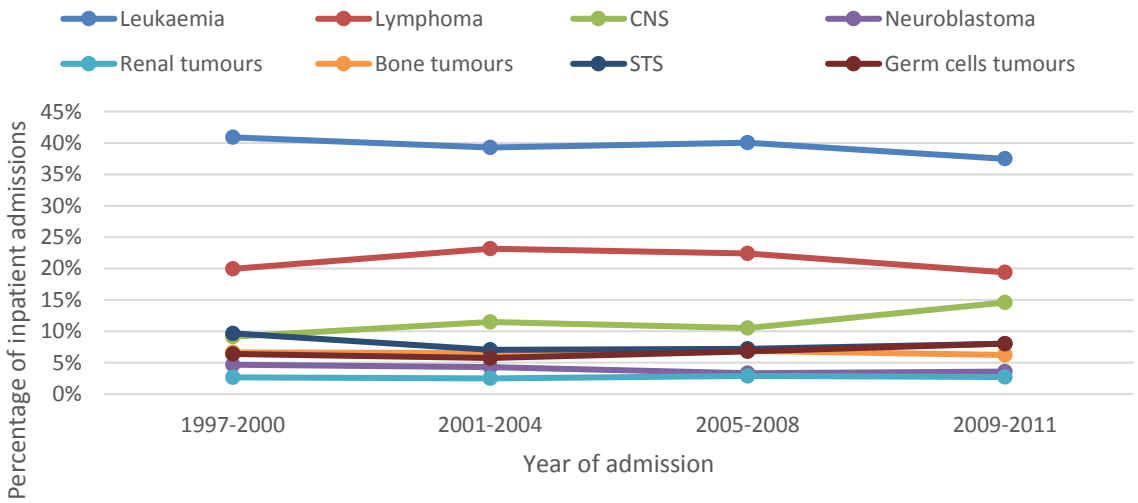


Figure 27: Percentage of inpatient hospital encounter by period of admission and diagnostic group

6.2.1.4 Distribution of admissions by year of diagnosis and diagnostic group (ICCC-3)

The percentage of admissions by year of diagnosis were assessed to determine whether the differences in documentation of admission varied by time of diagnosis (Figure 28). Cases diagnosed in 1996 (3%) had the lowest percentage of admissions and that could be justified by the quality of documentation during that period. The linkage of HES data became available from March 1997, so admissions before 1997 were not available in the requested data warehouse. The trend in admissions was not stable during the diagnosis period, as it began to increase after 1996, then decrease in 1999 and return to increase to reach its peak in 2001 with 9% of total admissions and then decreased in 2003 with 8%. After that the percentage of admissions increased to reach the highest point of 10% in 2005. These changes could represent the level of cancer incidence during each year, where 2001 and 2005 had the highest cancer incidence having 304 and 205 per million person-years (Section 5.3).

Additionally, these changes could be related to changes in treatment intensity, as the majority of the study, saw the main cancers such as leukaemia having more intensive treatment during the twenty-first century, as explained earlier in Chapter 2.

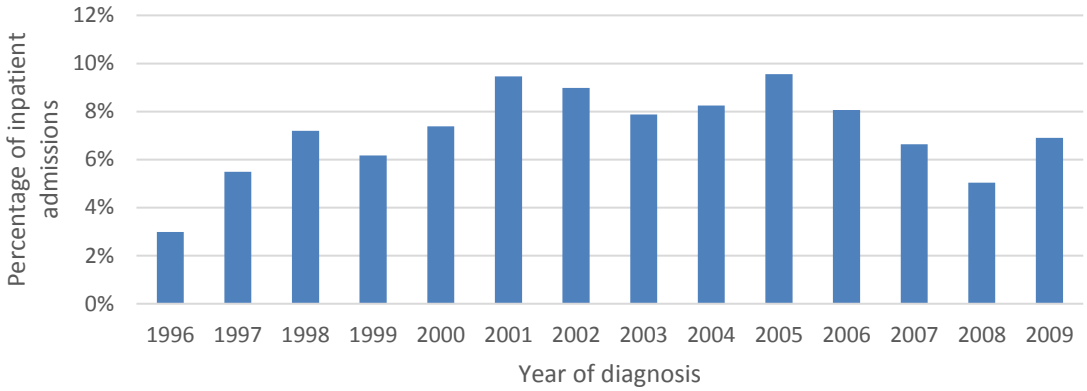


Figure 28: Percentage of admissions by year of diagnosis

6.2.1.5 Distribution of inpatient admissions by type of admissions (elective and emergency), gender and age in years

The distribution of admissions was assessed by gender and method of admission for comparative purposes with other published papers, and to check the capability of the current analysis to reflect nationwide hospital activity. The recurrent admissions in 2009 among CYP (aged 0-24 years during admission) was analysed in previous studies [201]. They found the number of emergency admissions was higher among children aged <1 when admitted, compared to people aged under 24.

The percentage of inpatient admissions by age at diagnosis showed that the rate of admission decreased with age. Rates of admission by age demonstrated two clear peaks: first around the age of one and the second at the age of three to four years for emergency admissions, and they were also higher among boys than girls (Figure 29). The rate of emergency admissions peaked among cases aged three years.

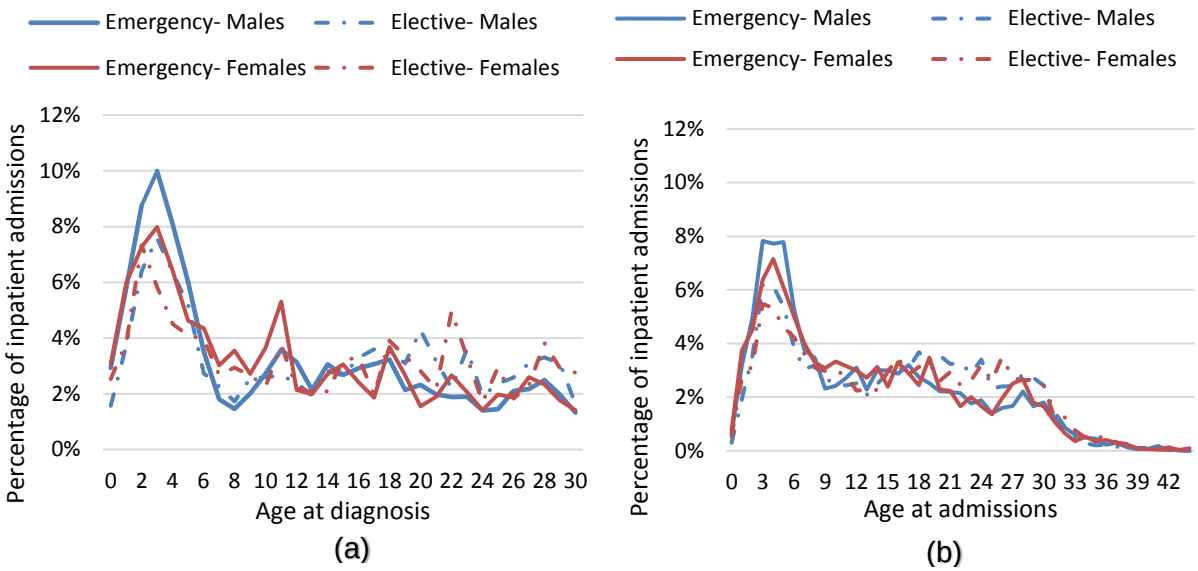


Figure 29: Percentage of admissions by age (years) at diagnosis (a) and age at admission (b), admission type and gender (1996-2011)

6.2.1.6 Distribution of inpatient admissions by diagnostic group

The number of inpatient admissions during 1996-2011 for individuals aged 0-29 at diagnosis were highest among patients diagnosed with leukaemia (median=38, IQR=17-55), followed by patients diagnosed with bone tumours (median=28, IQR=12-38), compared with other diagnostic groups (Figure 30).

Children diagnosed at the age 0-14 with leukaemia had higher numbers of inpatient admissions (median=44, IQR=30-58), followed by bone tumours (median=35, IQR=19-43) compared with other diagnostic groups (Figure 31 a). Individuals aged 15-29 years had higher numbers of admissions when diagnosed with bone tumours (median=23, IQR=10-32), followed by leukaemia (median=20, IQR=10-42), compared with other diagnostic groups (Figure 31 b).

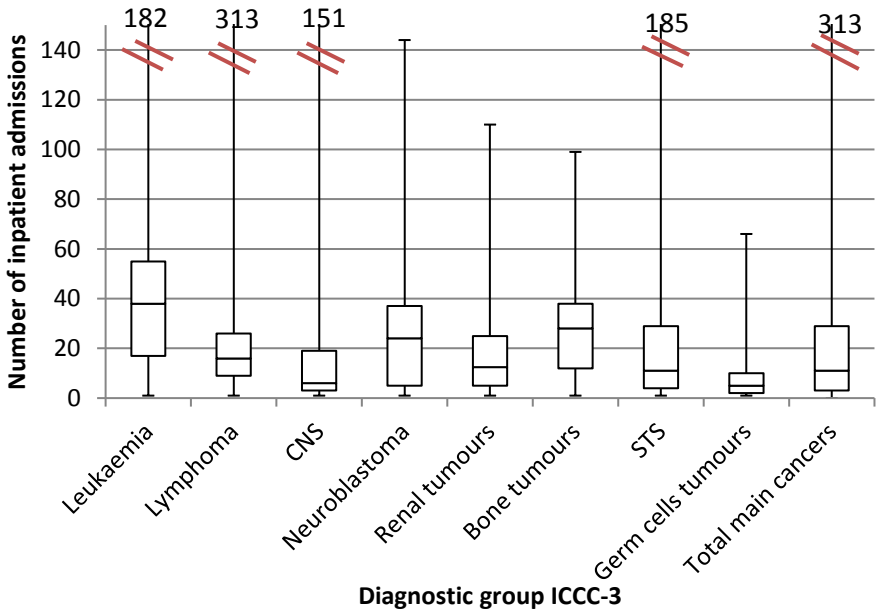


Figure 30: Number of inpatient post diagnosis admissions by main diagnostic group for cases aged 0-29 years

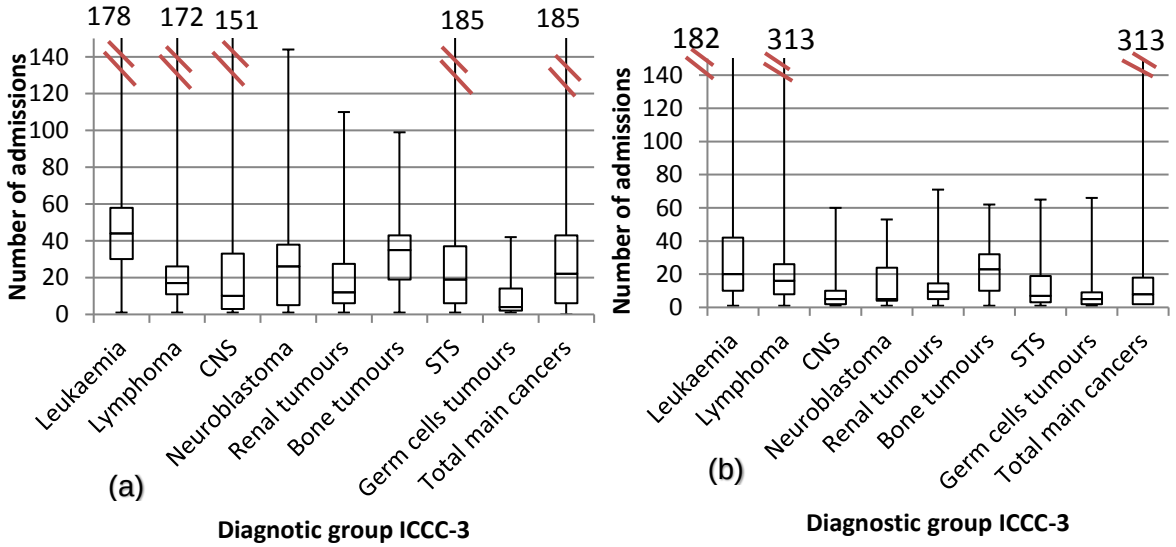


Figure 31: Number of inpatient post diagnosis admissions by main diagnostic group for cases aged 0-14 years (a) and 15-29 years (b) at diagnosis

6.2.1.7 Median rate of admission

6.2.1.7.1 Median inpatient admission rate per person-years and diagnostic group

The median rate of admission per person-year was almost 12 times higher during the on treatment phase compared with the post-treatment phase (Figure 32). Overall, the rate of admission was higher for individuals diagnosed with leukaemia and neuroblastoma, followed by bone tumours during the post diagnosis period, with medians of 6.4, 4.7 and 5.8 per person-year compared with other diagnostic groups. During the on treatment

phase, admission rates were significantly higher for cases with bone tumours (*p*-value<0.001), with a median of 16 admissions per person-year. Children had significantly higher median rate of admissions than TYA during treatment phase (median= 16.2 and 9.10 per person-year respectively, *p*-value<0.001) and after treatment phase (median=0.64 and 0.39 per person-year respectively, *p*-value<0.001).

Among children, the median rate of admissions was significantly higher for cases diagnosed with bone tumours, in both the on treatment and post-treatment phase, compared with other diagnostic groups, resulting in 21 and 1.6 admissions per person-years during these phases, respectively (*p*-value <0.001) (Figure 33 a).

The median rate of admissions per person-year was significantly higher among cases diagnosed with leukaemia and bone tumours among TYAs during the on treatment phase, with a median of 14 admissions per person-year (Figure 33 b). During the post-treatment phase, the median rate of admissions was higher for patients surviving from both neuroblastoma, leukaemia and bone tumours, compared with other diagnostic groups, with around one admission on average per person-year.

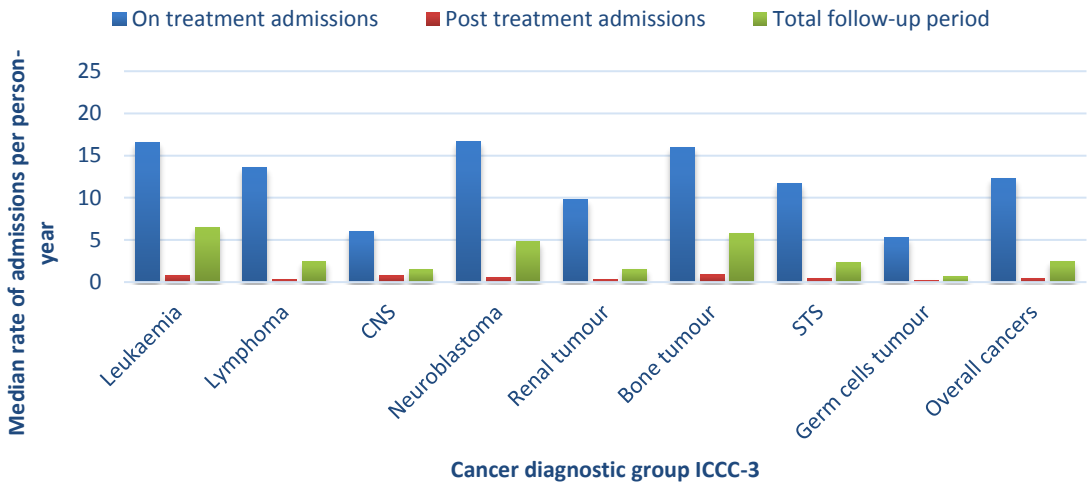


Figure 32: Median rate of inpatient admissions per person-years by admission period and diagnostic group

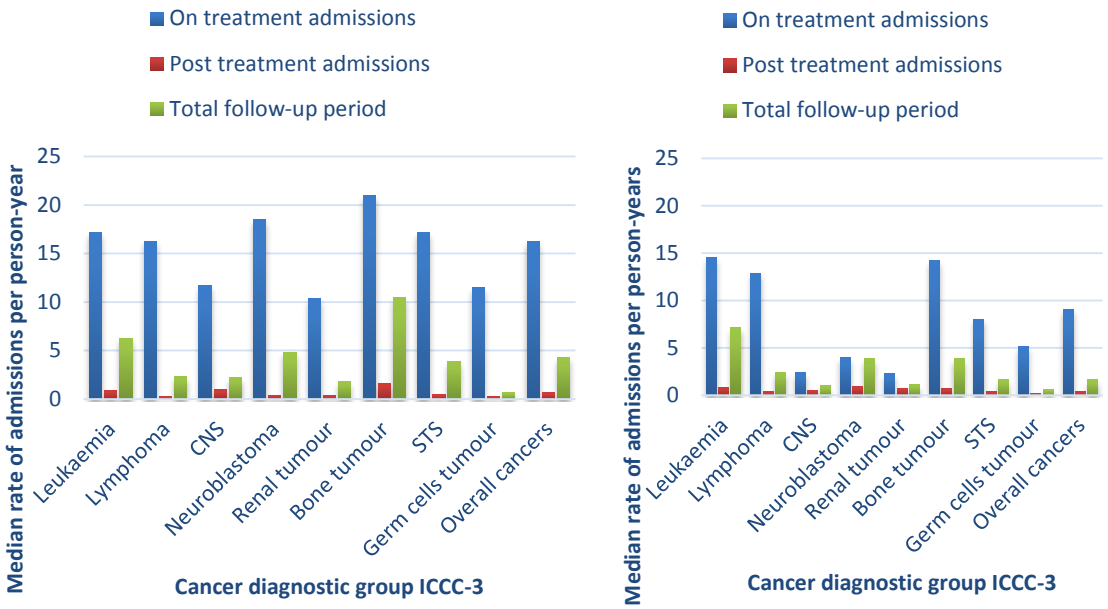


Figure 33: Median rate of inpatient admissions per person-years by admission period and diagnostic group for children aged 0 -14 (a) and aged 15-29 (b) years at diagnosis

6.2.1.7.2 Median inpatient admission rate per person-years, diagnostic group and gender

The median rate of admissions was higher among males compared with females, except for lymphoma and germ cell tumours (Figure 34).

There was a slight excess in the number of inpatient admissions among females compared with males, *p*-value<0.001, 2 compared with 2.5 median admissions per person-year, respectively (Figure 34). Overall, the rate of admissions was higher among females than males, which could be related to the follow-up years, males being followed up for longer periods than females, having 12,944.32 compared with 9,159.684. Without adjusting for person-year, males had higher numbers of admissions compared with females.

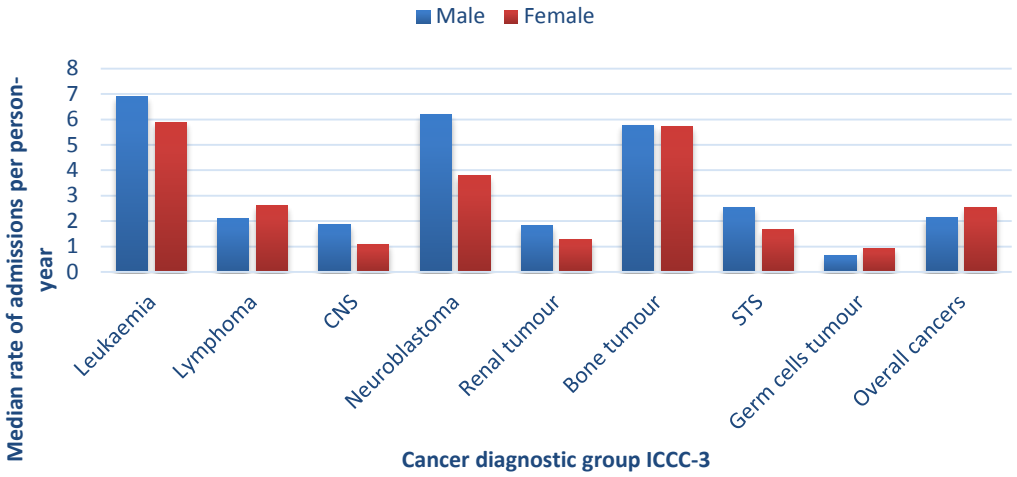


Figure 34: Median rate of admission per person-year by diagnostic group and gender

6.2.1.7.3 Median inpatient admission rate per person-years, diagnostic group and ethnicity

South Asian individuals had higher median rates of inpatient admissions than non-South Asians during the admission period 1997-2011 for the majority of diagnostic groups, except for STS (Figure 35). The difference in admission rates was most pronounced among renal tumours and STS. South Asians with renal tumours appeared to have more than double the rate of inpatient admissions compared with non-South Asians and three-times higher admission rates when diagnosed with germ cell tumours. In contrast, non-South Asians diagnosed with STS experienced three-times higher admission rates compared to South Asians.

The common morbidities leading to hospital admissions were compared by ethnicity and it was found that South Asians had fewer admissions for neoplasm purposes, compared with non-South Asians (67% compared with 76%, respectively, of the total causes of admissions) – data not shown.

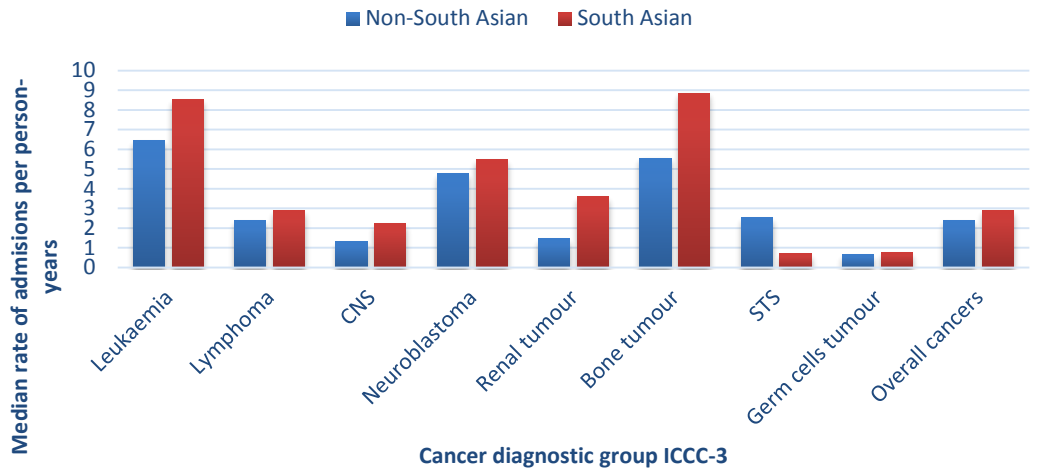


Figure 35: Median rate of admission per person-years by diagnostic group and ethnicity

6.2.1.7.4 Median inpatient admission rate per person-years, diagnostic group and deprivation

The rate of inpatient admissions was slightly higher among cases living in the least deprived areas compared to those from the most deprived areas for all cancers combined. However, the pattern differed by cancer type, as the most deprived cases with CNS tumours, leukaemia, lymphoma and renal tumours had the higher rates of admissions than least deprived cases (Figure 36).

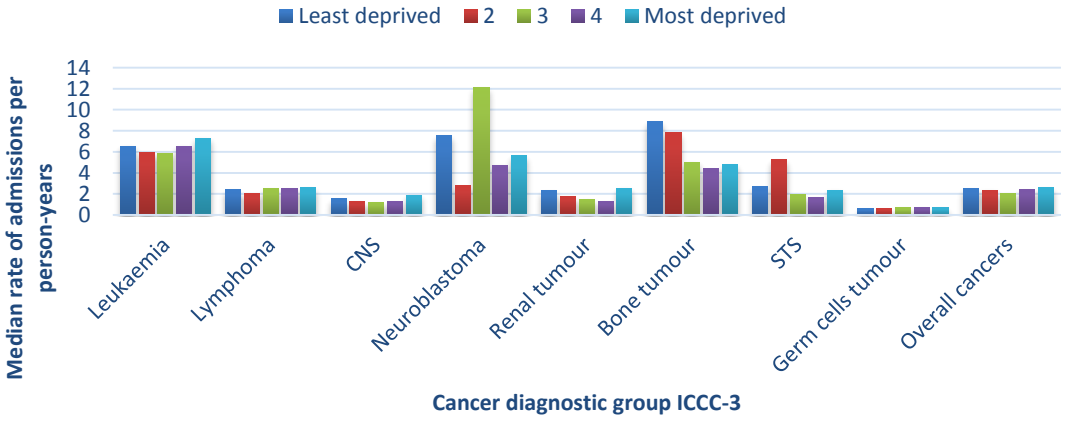


Figure 36: Median rate of admission per person-years by diagnostic group and deprivation category

6.2.1.7.5 Median inpatient admission rate per person-years, diagnostic group and relapsed.

The rate of inpatient admissions was higher among cases with relapses of the disease compared with non-relapsed cases for the majority of diagnostic groups (median=9 vs 2 admissions per person-year) (Figure 37).

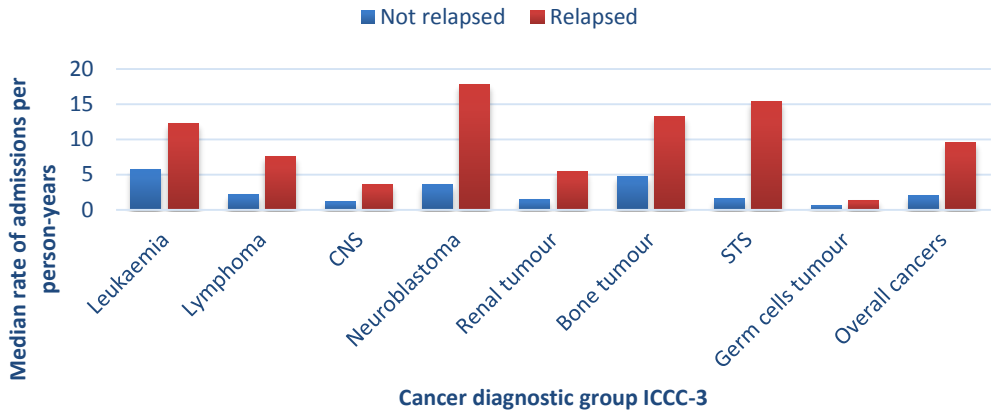


Figure 37: Median rate of admission per person-years by diagnostic group and relapse status

Further analysis was carried out to examine the rate of relapse by time in months since diagnosis for the three most common diagnostic groups: leukaemia, lymphoma and CNS tumours. Bone tumours were also examined further, as this group had the highest number of cases with relapses of the disease.

The median number of inpatient admissions for leukaemia cases with relapses began to increase 12 to 15 months after the date of diagnosis and continued to increase, exceeding the rate of inpatient admissions among non-relapsed cases (Figure 38). Lymphoma relapsed cases had higher rates of admission than non-relapsed cases from the date of diagnosis up to and beyond 4 years follow-up (Figure 39). CNS tumour admission rates were higher from the date of diagnosis among relapsed cases compared with non-relapsed cases and decreased 16 to 19 months after diagnosis (Figure 40). Despite the fact that the number of admissions among CNS cases was similar among non-relapsed and relapsed cases, using the number of days spent in hospital, the pattern of hospital activity was higher among relapsed compared with non-relapsed cases through the follow-up months.

For bone tumours, relapsed cases exceeded the number of admissions on average from date of diagnosis, compared to non-relapsed cases, then decreased thereafter to be equivalent to the non-relapsed cases 12-14 months after diagnosis. Admission rates fluctuated and peaked at two points 16-18 months and 28-31 months after diagnosis, then more than 48 months post diagnosis (Figure 41).

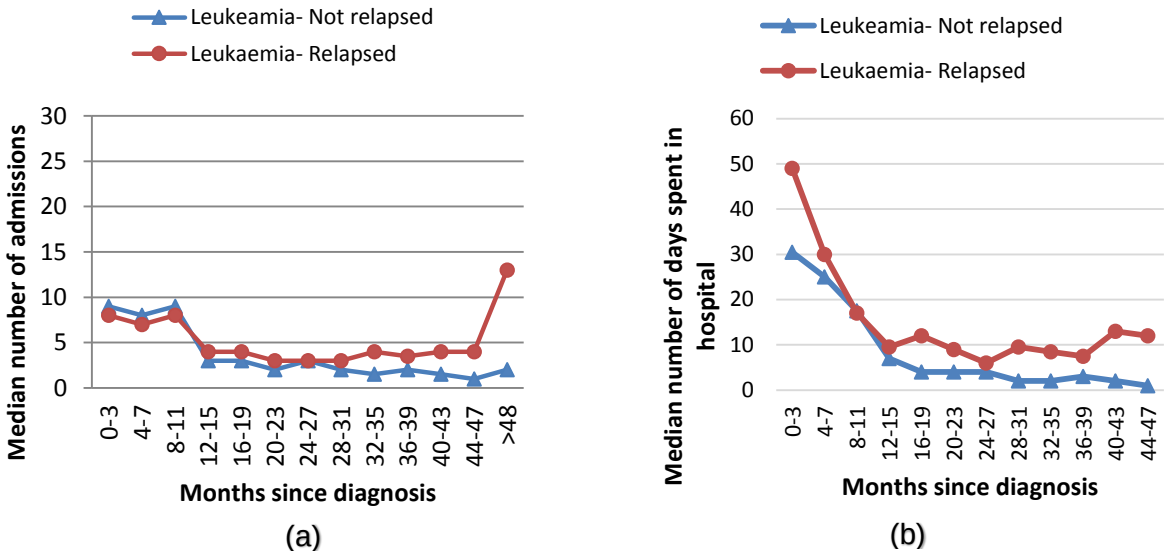


Figure 38: Distribution of median number of inpatient admissions(a) and number of days (b) by months since diagnosis and relapsed for leukaemia survivors diagnosed from 1996-2009

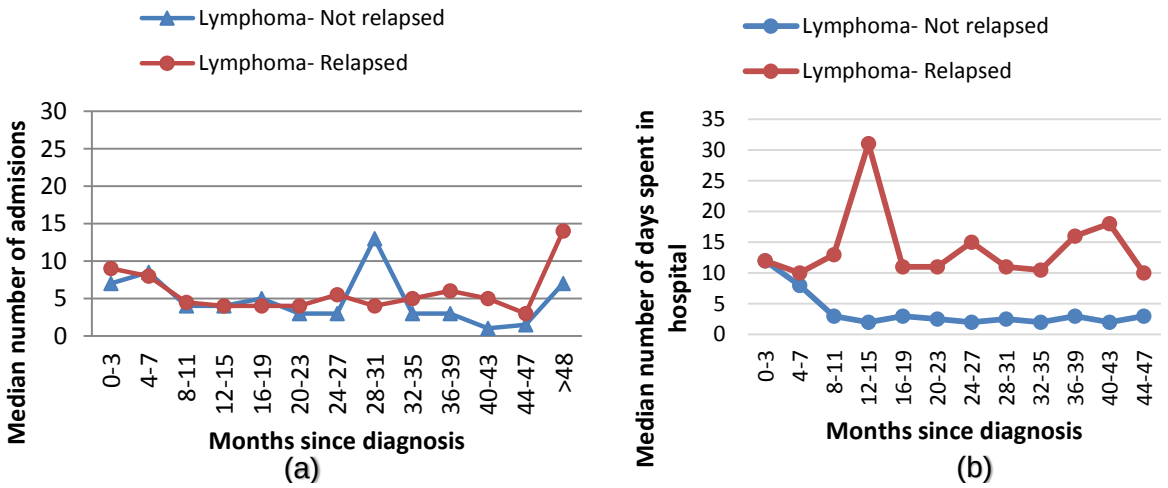


Figure 39: Distribution of median number of inpatient admissions(a) and number of days (b) by months since diagnosis and relapse status for lymphoma survivors diagnosed from 1996-2009

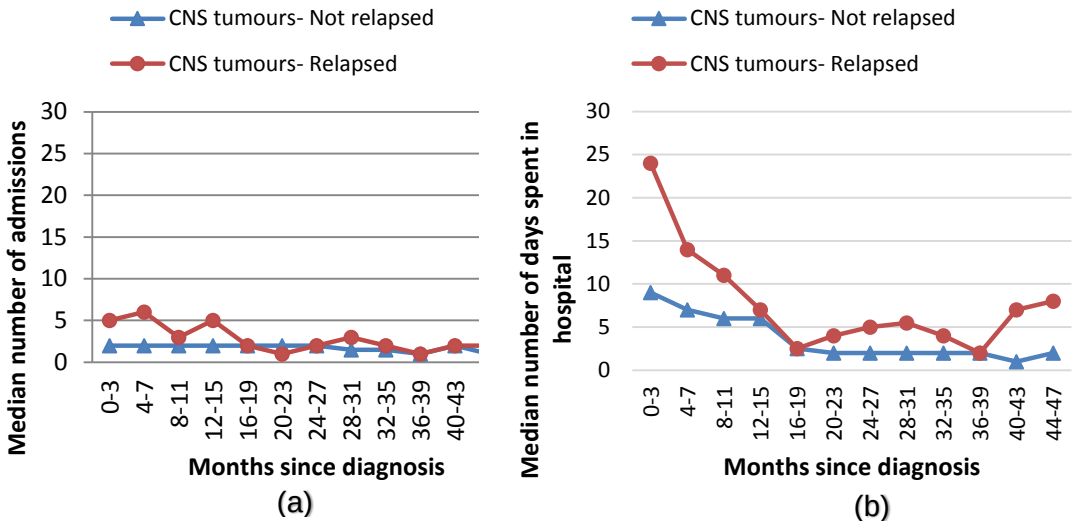


Figure 40: Distribution of median number of inpatient admissions (a) and number of days (b) by months since diagnosis and relapse status for central nervous system tumours diagnosed from 1996-2009

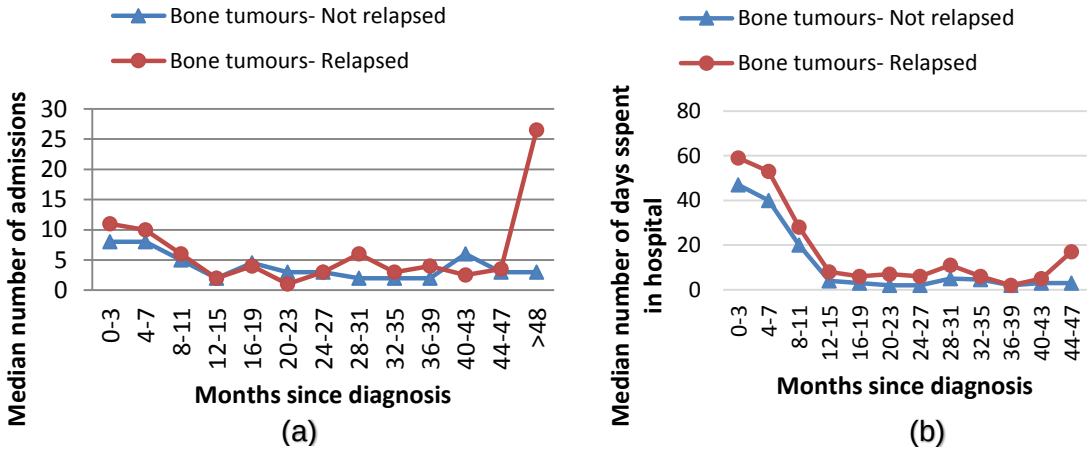


Figure 41: Distribution of median number of inpatient admissions (a) and number of days (b)by months since diagnosis and relapse status for bone tumours survivors diagnosed from 1996-2009

The pattern of post diagnosis inpatient admissions in months was assessed before and after the time of relapse, in order to check the general pattern of inpatient admissions for selected diagnostic groups (leukaemia, lymphoma and bone tumours). The median number of inpatient admissions increased sharply around the time of relapse, and decreased sharply thereafter (Figure 42).

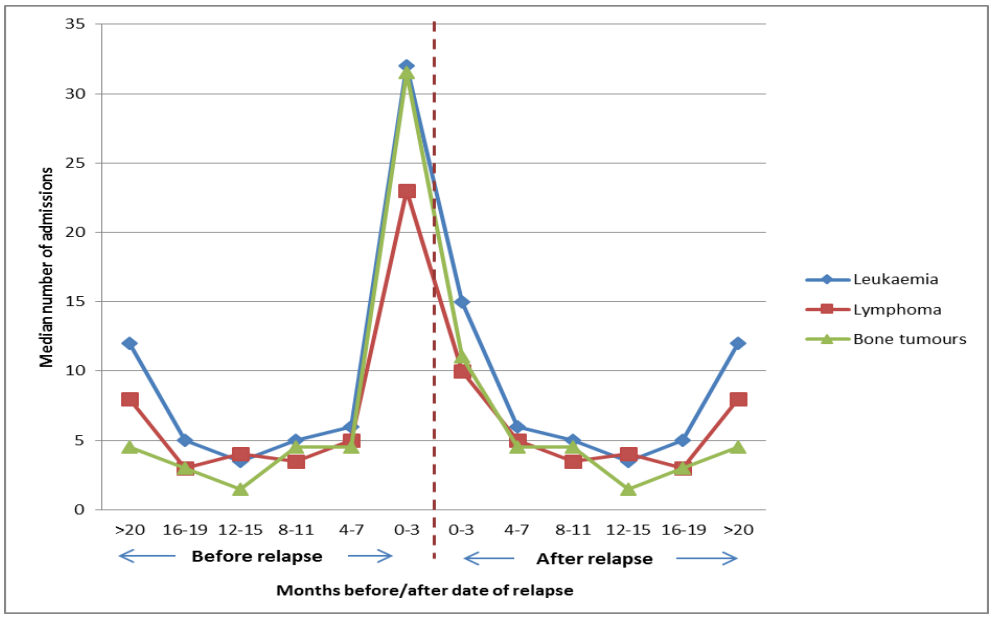


Figure 42: Distribution of median number of inpatient admissions by months since diagnosis before and after relapse for relapsed cases diagnosed 1996-2009

The trajectories of admissions were assessed from the date of relapse to the end of the follow-up period among survivors with relapses, compared with non-relapsed survivors for selected cancer types. This was done to answer clinical concerns among relapse survivors, especially leukaemia survivors who might be in severe need of hospital care within a year of relapse. Additionally, in earlier sections, the admissions among relapsed survivors were almost double the median number of admissions for non-relapsed survivors, especially one year following the date of diagnosis for leukaemia, lymphoma and CNS tumour survivors. It was necessary to assess whether the difference in admissions among relapsed survivors was consistent during the follow-up period preceding the date of relapse, compared with non-relapsed survivors where the date of diagnosis was used instead.

Relapsed leukaemia survivors had a lower median number of admissions 11 months following the date of relapse than non-relapsed cases, then the median number of admissions became higher among relapsed survivors compared to non-relapsed survivors in the 12 to 31 months following the date of relapse/diagnosis. However, these differences were modest – one or two admissions within a three-month period between both groups (Figure 43). While, in terms of length of stay, relapsed survivors stayed for almost double the length of non-relapsed survivors during the first three months after the date of relapse/diagnosis.

Lymphoma survivors had the highest admissions and lengths of stay among relapsed survivors, compared with non-relapsed survivors preceding the date of relapse/diagnosis from 11 to 48 months (Figure 44). The pattern fluctuated and the gap was wider 24-27

months following the date of relapse/diagnosis, with seven compared with one admission, on average, for relapsed and non-relapsed survivors. Similarly, 24 to 31 months after relapse/diagnosis, relapsed survivors had a five-fold longer stay than non-relapsed survivors.

The difference of number of admissions and length of stay was modest between relapsed and non-relapsed CNS tumour and bone tumour survivors following the date of relapse/diagnosis (Figure 45 and Figure 46).

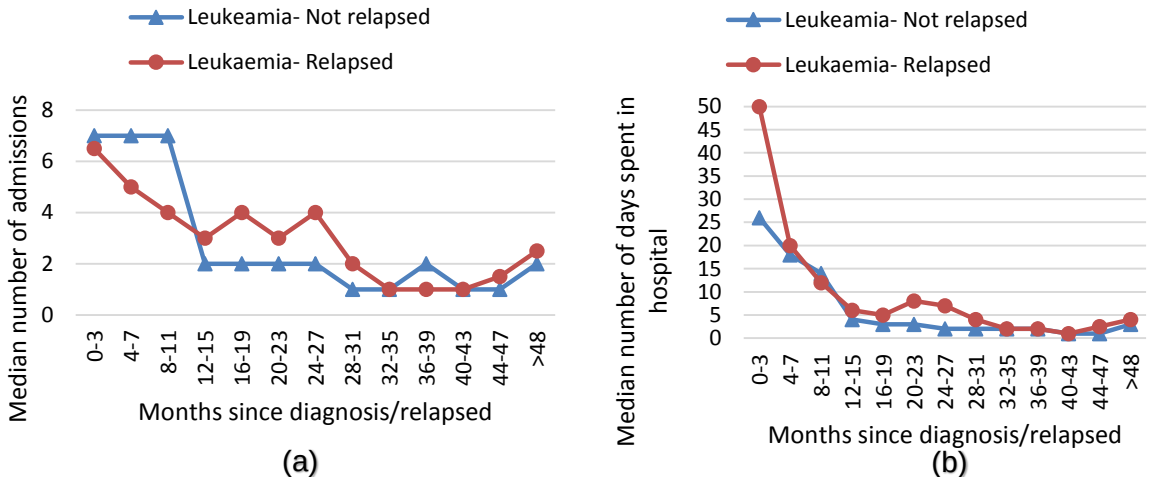


Figure 43: Distribution of median number of inpatient admissions(a) and number of days (b) by months since diagnosis/relapse and relapsed status for leukaemia survivors

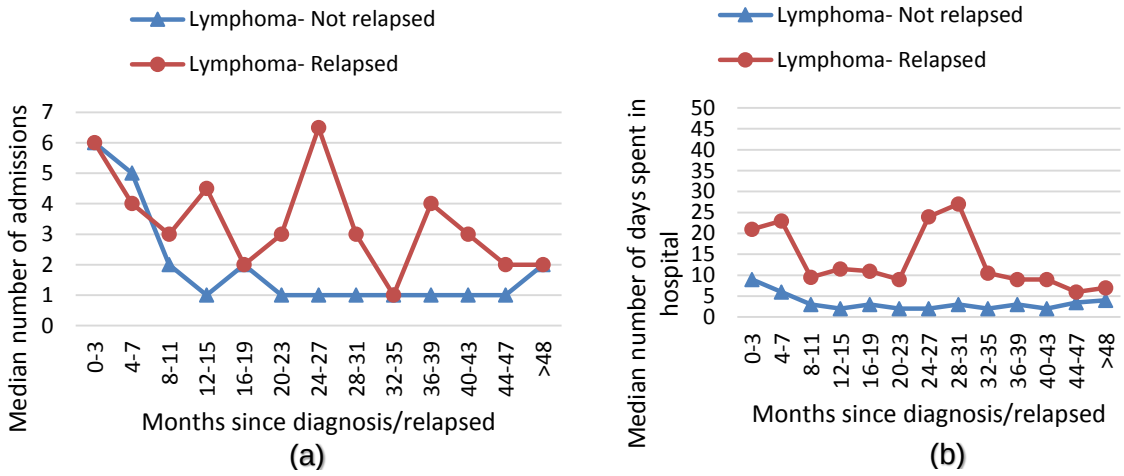


Figure 44: Distribution of median number of inpatient admissions(a) and number of days (b) by months since diagnosis/relapse and relapsed status for lymphoma survivors.

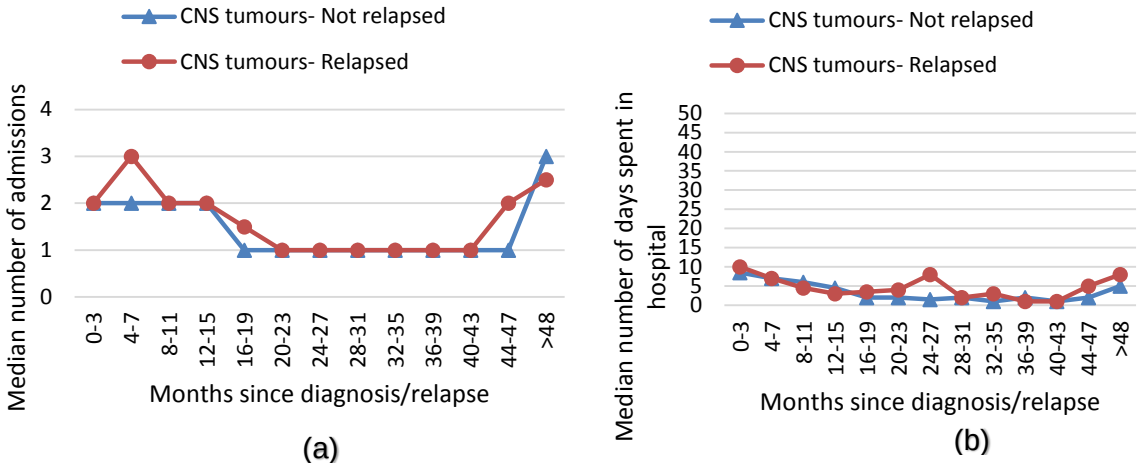


Figure 45: Distribution of median number of inpatient admissions(a) and number of days (b) by months since diagnosis/relapse and relapsed status for CNS tumours survivors

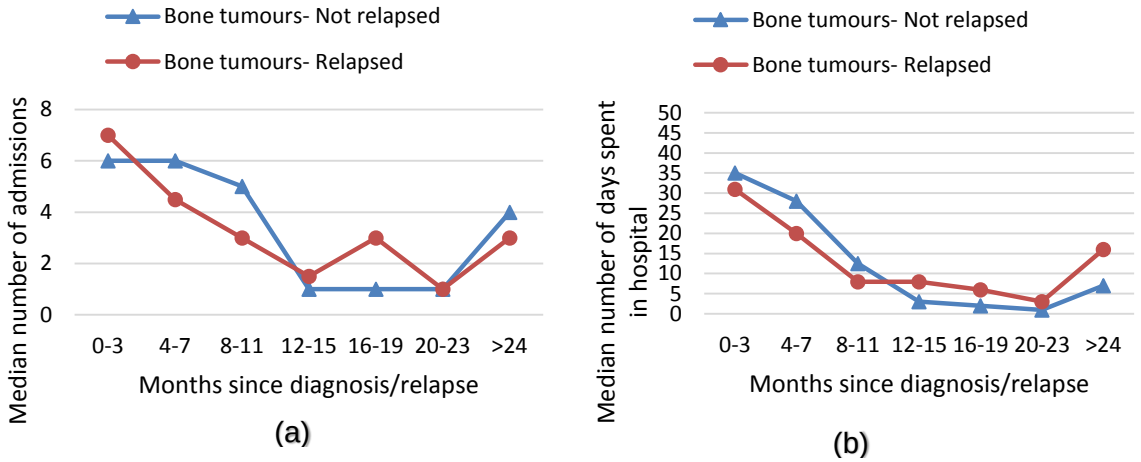


Figure 46:Distribution of median number of inpatient admissions(a) and number of days (b) by months since diagnosis/relapse and relapsed status for bone tumours survivors

In this part of the analysis, the trend in admissions among relapsed cases by year of admission were checked to monitor the proportion of relapsed cases each year. In Figure 47, the proportion of admissions steadily decreased by year of diagnosis from 0.31 admissions in 1997 to 0.16 admissions in 2011, reflecting a decrease in the percentage of relapsed cases in each year.

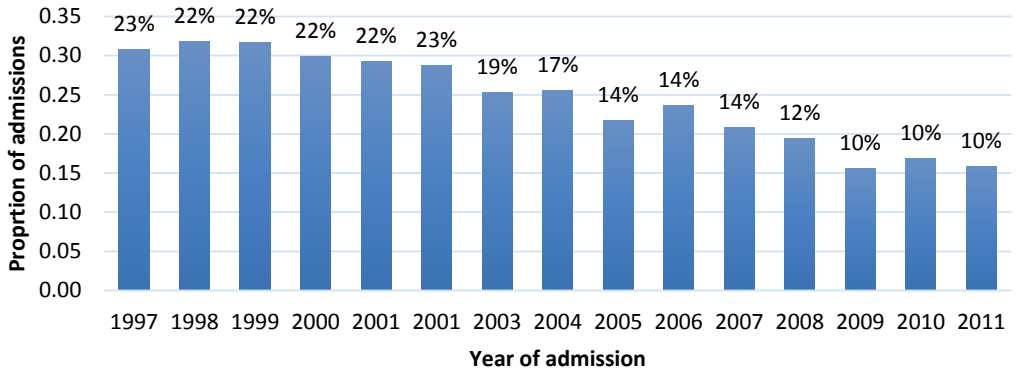


Figure 47: The trend in proportion of admissions and percentage of cases with relapses by year of admission

6.2.1.8 Death during follow-up period

The pattern of admission, as discussed in Chapters 2 and 3, could be higher among cases that do not survive the first five years after diagnosis. The pattern of hospital admissions could be higher toward the end of life due to complexity of the disease and its treatment. Out of 2,867 cases, 595 (21%) died during the study period, with the time to death ranging between 0 and 14 years following the date of diagnosis, with a median of 1.5 years. The trajectory of admissions censored at four years before the date of death reflect that the median number of admissions saw a slight increase from seven to nine admissions, between three and one year prior to death (Figure 48).

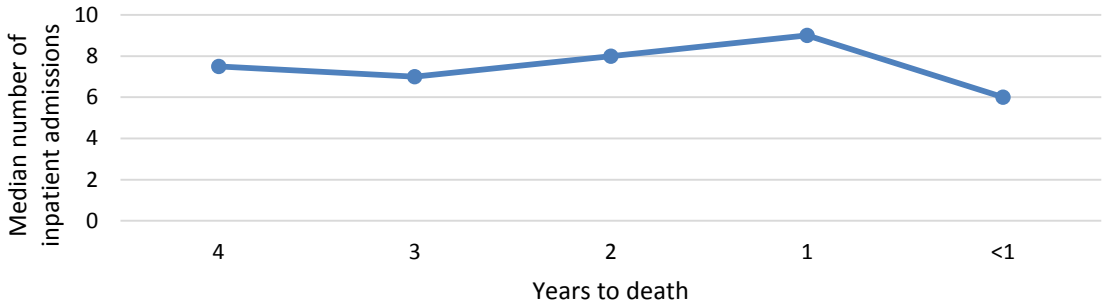


Figure 48: Median number of admissions by time to death in years for all cancer in combined

6.2.1.9 Distribution of cases / admissions during follow-up period and diagnostic group

The distribution of cases based on period of admission is illustrated in Table 30, to understand the frequency of health services, given the number of cases that contributed in each period. The rate of admission by person-years decreased during the admission period from diagnosis until the end of follow-up period and began to increase again more than eight years following treatment completion (Figure 49, Figure 50).

Table 30: Number of cases by period of admission (on treatment and post-treatment) and main diagnostic group

Cancer types ICCC-3	Children					TYA				
	On treatment	0-2 years post-treatment	3-4 years post-treatment	5-7 years post-treatment	⩾8 years post-treatment	On treatment	0-2 years post-treatment	3-4 years post-treatment	5-7 years post-treatment	⩾8 years post-treatment
Leukaemia	408	303	60	54	34	200	101	40	22	15
Lymphoma	142	72	22	25	17	454	203	110	99	68
CNS	237	152	79	72	43	173	90	49	36	24
Neuroblastoma	80	42	11	9	#	9	6	<5	<5	0
Renal tumours	73	46	16	13	10	10	10	#	<5	5
Bone tumours	53	23	9	6	<5	94	42	17	22	9
STS	100	51	18	19	18	123	48	22	27	20
Germ cell tumours	49	37	14	19	17	440	151	74	83	60
Overall cancers	1,142	726	229	217	148	1,503	651	320	293	201

Abbreviations: CNS = central nervous system; STS = soft tissue sarcoma
figures removed to avoid disclosure of potentially identifiable data

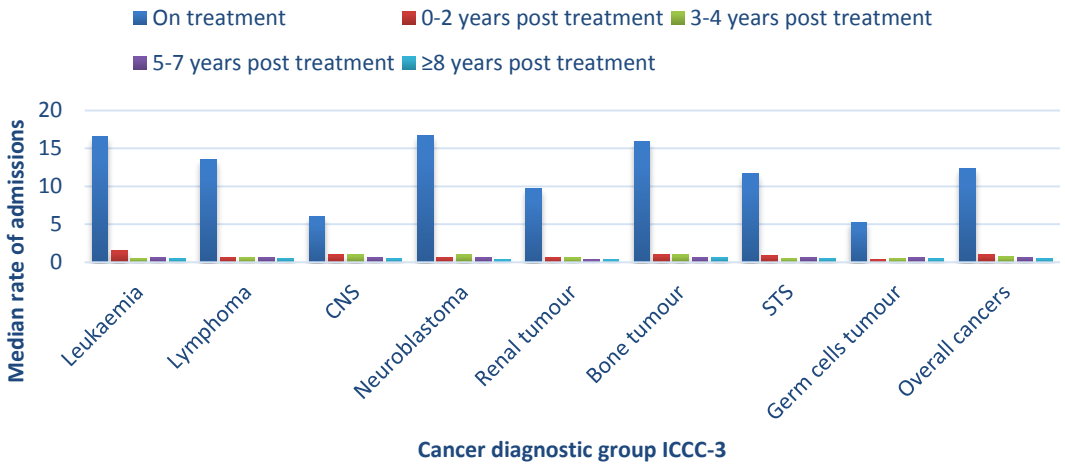


Figure 49: Median rate of admission per person-years for individuals aged 0-29 at diagnosis by follow-up period and diagnostic group

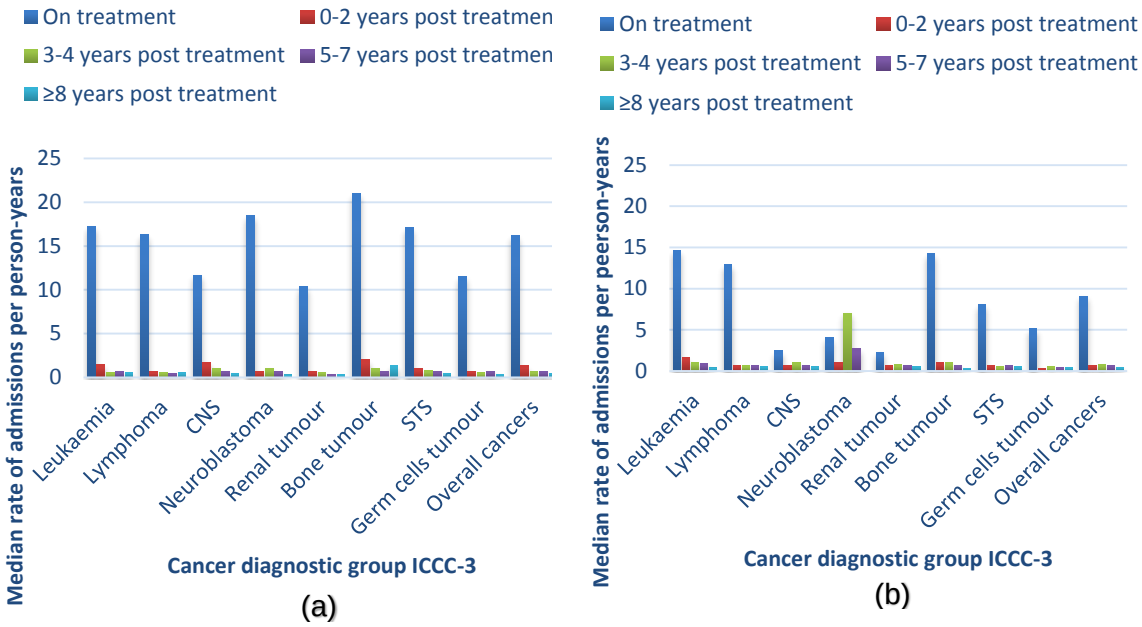


Figure 50: Median rate of admission per person-years for individuals aged 0-14 (a) and 15-29 (b) at diagnosis by follow-up period and diagnostic group

6.2.1.10 Number of admissions by level of specialist care

The proportion of survivors with specialist admissions varied by cancer type and age group; children had a higher proportion of their admissions in specialist units than TYAs after being diagnosed with cancer (Section 5.3.3.5). The median rate of admission by level of specialist intake was analysed during treatment and after treatment completion for the main cancer types. This was done to understand whether differences in the admission rates were consistent in the treatment phase and post-treatment phase. The significant difference in admissions between cases with mostly specialist care compared with cases with limited specialist care during the follow-up period was evident during the treatment phase. For all cancers combined, the median rate of admission for cases with mostly specialist care was 35 admissions, while for cases with limited specialist care it was 15 admissions. The difference was consistent by cancer type, however, survivors of lymphomas and germ cell tumours had similar median numbers of admissions for cases with mostly specialist and limited specialist care (Table 31). The median number of admissions, similarly, was higher among cases receiving the majority of their care in specialist units, compared to cases that had limited specialist care with different types of treatment. Survivors treated with chemotherapy had, on average, a higher number of admissions compared with other treatment types (Table 32).

Table 31: Number of admissions, median and interquartile rage by level of specialist care and admission period

Cancer types	Total period					On treatment					Post-treatment				
	Admissions	Person-years	Median number of admission	IQR		Admissions	Person-years	Median	IQR		Admissions	Person- years	Median	IQR	
Leukaemia															
Limited specialist care	3,310	661	15	8	35	2,548	630	11	6	25	762	465	5	2	15
Some specialist care	2,190	580	29	13	47	1,818	580	24	10	38	372	4351	4	2	9
Mostly specialist care	19,002	2,904	43	28	58	16,525	2,897	38	24	51	2,477	1,8881	5	3	8
Lymphoma															
Limited specialist care	6,713	2,765	15	6	24	5,089	2,653	14	7	21	1,624	2,201	2	1	6
Some specialist care	599	311	11	6	28	361	307	9.5	5	18	238	270	6	2	12
Mostly specialist care	6,129	1,815	18	12	27	4,833	1,814	15	10	23.5	1,296	1,463	2	1	8
CNS															
Limited specialist care	1,164	1,009	4	2	8	679	680	3	1	6	485	515	2.5	1	6
Some specialist care	742	470	5	3	11	518	333	4	2	9	224	219	3	2	5
Mostly specialist care	5,064	1,560	13	4	32	3,705	1,324	9	2	26	1,359	913	6	3	12
Neuroblastoma															
Limited specialist care	177	84	6	1	21	133	81	8	1	21	44	72	3.5	1.5	8.5
Some specialist care	58	29	5	4	9	43	29	5	1.5	20	15	24	3	3	3
Mostly specialist care	2,185	411	29	9	40	1,922	375	25.5	5	36	263	272	3	2	5
Renal tumours															
Limited specialist care	175	172173	4	1	10	60	173	2	1	6	115	152	3.5	1.5	7
Some specialist care	213	144	13	7	19	149	144	8	4	12	64	126	3	2	8
Mostly specialist care	1,278	436	15	8	30	1,043	435	15.5	8	27	235	363.6	2	1	5
Bone tumours															
Limited specialist care	373	219	6	2	18	265	167	3	2	13	108	119	3.5	2	9
Some specialist care	306	87	20.5	6.5	42	264	87	18	3	35	42	63	3	2	6
Mostly specialist care	3,425	559	30	21	40	3,064	552	27.5	19	35	361	353	4	1	8

Cancer types	Total period					On treatment					Post-treatment				
	Admissions	Person-years	Median number of admission	IQR		Admissions	Person-years	Median	IQR		Admissions	Person- years	Median	IQR	
STS															
Limited specialist care	477	529	5	2	12	333	419	4	1	10	144	382	3	2	5
Some specialist intake	507	256	6	3	24	405	231	6	2	17	102	184	3	1.5	7.5
Mostly specialist care	3,802	848	19	5	35	3,111	805	18.5	5.5	32	691	592	4	2	9
Germ cell tumours															
Limited specialist care	1,160	2,012	2	1	6	712	1,975	1.5	1	5	448	1,807	2	1	3
Some specialist care	605	570.24	5	2	10	410	543	2.5	2	8	195	480	2	1	4
Mostly specialist care	2,317	1,775	8	4	11	1,841	1,751	8	3	11	476	1,524	2	1	5
Overall cancers															
Limited specialist care	13,549	7,452	7	2	16	9,819	6,778	7	1	15	3,730	5,712	3	1	6
Some specialist care	5,220	2,446	9	3	22.5	3,968	2,253	8	2	20	1,252	1,800	3	2	7
Mostly specialist care	43,202	10,307	21	8	40	36,044	9,956	18	8	35	7,158	7,367	4	2	8

Abbreviations: CNS = central nervous system; STS = soft tissue sarcoma; IQR = interquartile range

Table 32: Number of admissions, median and interquartile range by level of specialist care, type of initial treatment and period of admissions

Type of treatment	Total period				On treatment				Post-treatment			
	Admissions	Median number of admission	IQR		Admissions	Median number of admission	IQR		Admissions	Median number of admission	IQR	
Chemotherapy												
Limited specialist care	11,803	14	7	24	8,949	12	6	20	2,854	3	1	8
Some specialist care	4,448	15	7	33	3,513	12	6	26	935	3	2	8
Mostly specialist care	41,115	26	13	44	34,983	22	11	38	6,132	4	2	8
Radiotherapy												
Limited specialist care	3,407	5	2	18	2,585	5	1	17	822	2	1	5
Some specialist care	812	9	3	18	593	7	2	13	219	4	2	6
Mostly specialist care	5,300	16	6	33	4,435	15	4	31	865	4	2	7
Surgery												
Limited specialist care	3,481	3	1	8	2,105	2	1	7	1,376	2	1	4
Some specialist care	1,674	5	3	12	1,164	3	2	8	510	3	1	5
Mostly specialist care	11,732	11	5	27	9,292	10	3	23	2,440	4	1	7

Abbreviations: IQR = interquartile range

6.2.2 Number of days spent in hospital

6.2.2.1 Median number of days by age at diagnosis and diagnostic group

Individuals diagnosed with bone tumours generally spent more time in hospital compared with other diagnostic groups (median=7.4 days per 100 person-days). Children spent more time in hospital compared with TYAs for the majority of diagnostic groups (median=3 vs 1 day per 100 person-days, respectively) except for individuals diagnosed with leukaemia (median=4 vs 8 days per 100 person-days for children and TYAs, respectively) and germ cell tumours (median=0.38 vs 0.44 days per 100 person-days for children and TYAs, respectively) (Figure 51).

During the treatment phase, individuals diagnosed with bone tumours spent more days in hospital compared with other diagnostic groups, around 29 days per 100 person-days on average, *p*-value<0.001. Children spent more time in hospital compared with TYAs for the majority of diagnostic groups (median=12 vs 6 days per 100 person-days, respectively, *p*-value<0.001), except for leukaemia (median=12 vs 27 days per 100 person-days for children and TYAs, respectively) (Figure 52).

During the post-treatment phase, individuals diagnosed with bone tumours and leukaemia spent more time in hospital compared with other diagnostic groups (median=0.4 and 0.32 days per 100 person-days, respectively). Children spent more time in hospital than TYAs (median=0.28 vs 0.21 days per 100 person-days, respectively), except cases diagnosed with lymphoma and bone tumours, however the differences between the number of days spent in hospital and age group were very small.

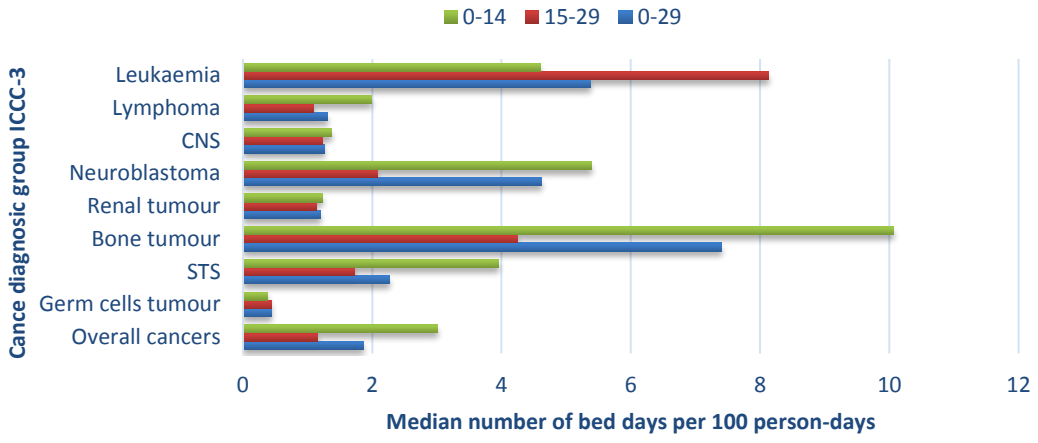


Figure 51: Median rate of number of days spent in hospital per 100 person-days during the admission period (1997-2011) by diagnostic group and age group

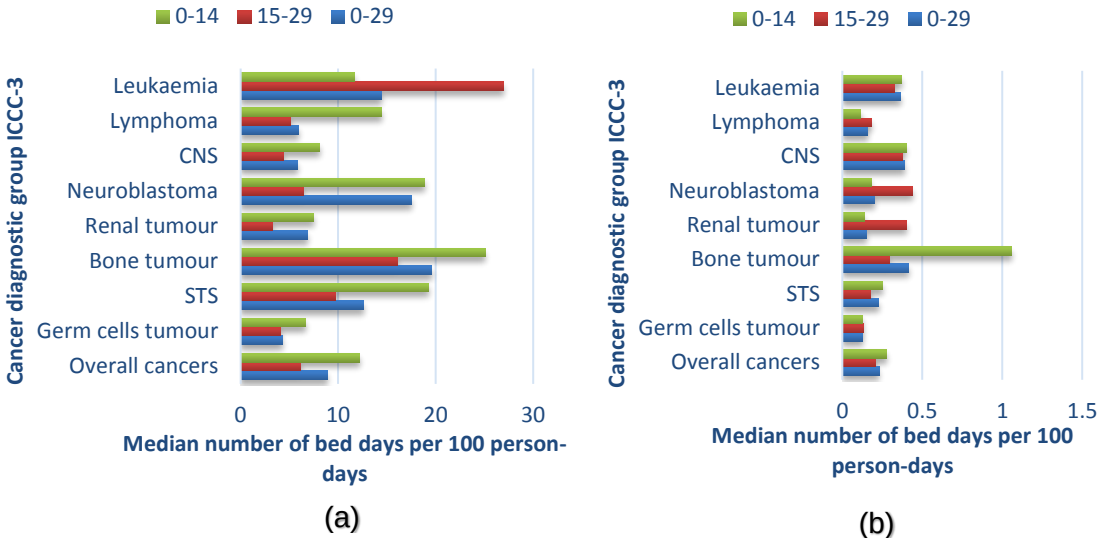


Figure 52: Median rate of number of days spent in hospital per 100 person-days during the on treatment phase (a), and post treatment (b) by diagnostic group and age group

6.2.2.2 Median number of days by follow-up period

The number of days patients spent in hospital generally decreased according to follow-up time for all diagnostic groups, except for bone tumours and renal tumours, as they started to increase eight years following the date of treatment completion (Figure 53 for all ages and Figure according to age group).

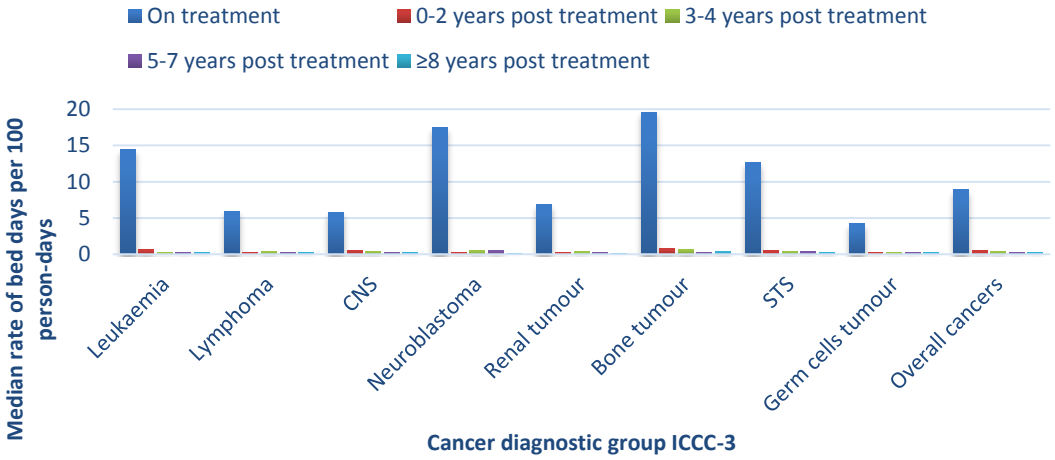


Figure 53: Median number of days patients aged 0-29 years at diagnosis spent in hospital per 100 person-days by diagnostic group and follow-up period since diagnosis

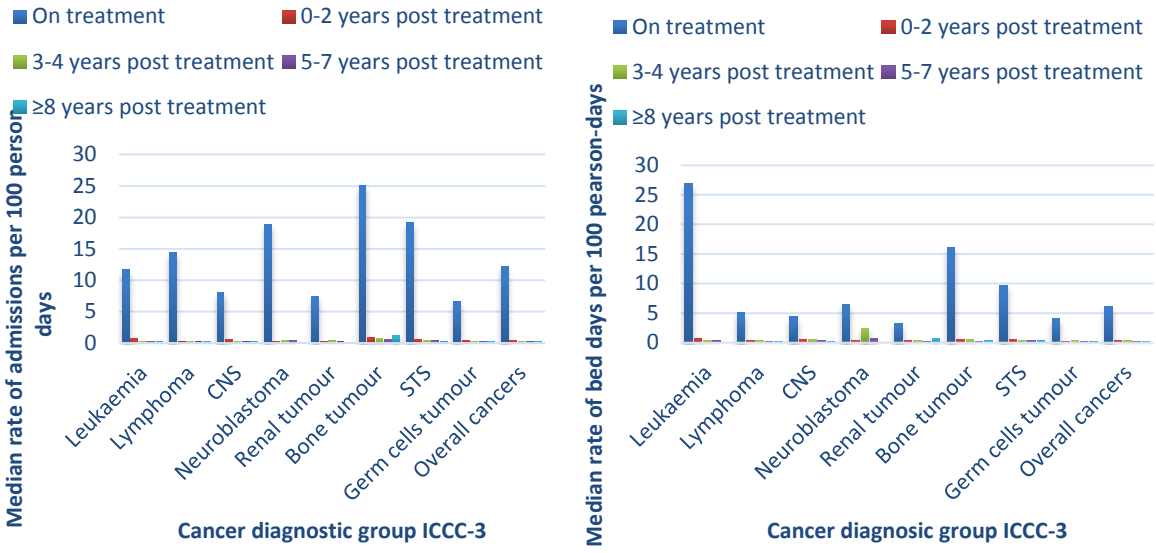


Figure 54: Median number of days patients aged 0-14 (a) and 15-29 (b) years at diagnosis spent in hospital per 100 person-days by diagnostic group and follow-up period since diagnosis

6.3 Outpatient admissions

The aim of the study was to analyse the healthcare burden among the cancer cohort, so as to monitor and improve their health outcomes. Cancer cases could receive care from both inpatient and outpatient services. Therefore, outpatients were analysed by linking outpatient admissions on HES with cancer registers for patients.

The information of outpatients was available from 2003 to 2011. Out of 2,861 survivors diagnosed 2003-2009, 2,831 (99%) survivors had linked outpatient records, when using date of birth, gender, NHS ID number and postcode at diagnosis. The percentage of outpatient admissions was calculated by dividing the total number of outpatient admissions for each specific cancer group by total outpatient admissions. Leukaemia cases accounted for 50% of total outpatient admissions among children (0-14), followed by CNS with about 16%, while each of the remaining diagnostic groups had lower than 10% of admissions (Table 33 and Figure 56). For TYAs, lymphoma cases had the highest percentage of admissions, followed by germ cell tumours.

For overall cancers, males had the higher number of outpatient encounters than females. Among children, males had a higher percentage of admissions than females, except for CNS tumours. Among TYAs, females had a higher percentage of outpatient admissions than males, except for leukaemia and germ cell tumours (Table 34). .

Table 33: Distribution of number of outpatient admissions by diagnostic group and age at diagnosis

	0-14				15-29				0-29			
Diagnostic group ICCC-3	**Number of cases**	**%**	**Number of events**	**%**	**Number of cases**	**%**	**Number of events**	**%**	**Number of cases**	**%**	**Number of events**	**%**
Leukaemia	371	33	30,181	50	244	12	9,627	19	615	20	40,959	36
Lymphoma	141	13	4,632	8	494	24	14,475	28	635	20	19,779	17
CNS	221	20	9,874	16	242	12	5,251	10	463	15	15,465	14
Neuroblastoma	67	6	2,475	4	29	1	334	1	96	3	2,834	2
Retinoblastoma	#	3	1,265	2	<5	0	0	0	#	1	1,265	1
Renal tumours	71	6	2,796	5	21	1	407	1	92	3	3,257	3
Hepatic tumours	13	1	730	1	15	1	174	0	28	1	904	1
Bone tumours	43	4	1,829	3	107	5	2,498	5	150	5	4,593	4
STS	86	8	3,717	6	166	8	3,133	6	252	8	7,015	6
Germ cell tumours	60	5	1,708	3	504	25	10,048	19	564	18	11,851	10
Other epithelial tumours	21	2	617	1	195	10	5,553	11	216	7	6,271	5
Other unspecified tumours	<5	0	91	0	#	0	212	0	#	0	303	0
Overall	1,128	100	59,915	100	2,023	100	51,712	100	3,151	100	114,496	100

Abbreviations: CNS = central nervous system; STS = soft tissue sarcoma

figures removed to avoid disclosure of potentially identifiable data

It was not possible to identify diagnosis at admission for the outpatient visit, as 99.5% of these admissions were coded as 'factors influencing health status and contact with health services'. Therefore, we had only estimates of the proportions of admissions by age group, gender and cancer type to understand the pattern of admission among cancer survivors, in terms of outpatient visits with the previously described inpatient admissions. Furthermore, it was not possible to identify the treatment received during their visit, whether it was to receive treatment or due to suffering from treatment complications. This was due to coding issues.

Table 34: Distribution of number of outpatient admissions by diagnostic group, age at diagnosis and gender

Diagnostic group ICCC-3	0-14				15-29			
	Male		Female		Male		Female	
	N	%	N	%	N	%	N	%
Leukaemia	17,797	50%	13,535	49%	5,509	20%	4,118	17%
Lymphoma	3,161	9%	2,143	8%	6,832	24%	7,643	32%
CNS	5,204	15%	5,010	18%	2,207	8%	3,044	13%
Neuroblastoma	1,337	4%	1,163	4%	217	1%	117	0%
Retinoblastoma	746	2%	519	2%	<5	0%	<5	0%
Renal tumours	1,716	5%	1,134	4%	240	1%	167	1%
Hepatic tumours	468	1%	262	1%	75	0%	99	0%
Bone tumours	1,081	3%	1,014	4%	1,443	5%	1,055	4%
STS	2,425	7%	1,457	5%	1,512	5%	1,621	7%
Germ cell tumours	987	3%	816	3%	8,637	31%	1,411	6%
Other epithelial tumours	369	1%	349	1%	1,267	5%	4,286	18%
Other unspecified tumours	<5	0%	90	0%	<5	0%	212	1%
Overall	35,292	100%	27,492	100%	27,939	100%	23,773	100%

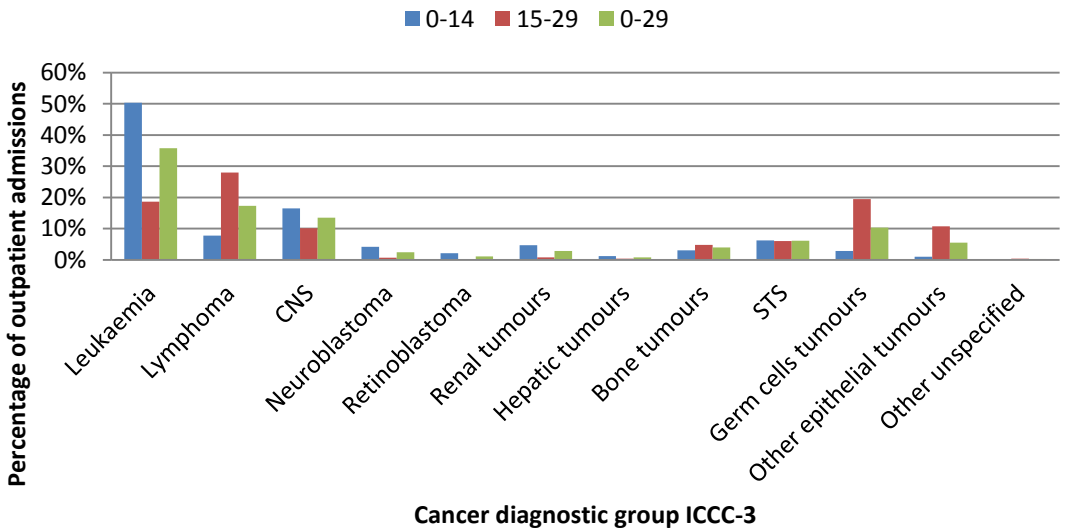


Figure 55: Distribution of outpatient admissions by diagnostic group and age at diagnosis

The median number of outpatient admissions was higher among leukaemia survivors compared with other cancer types, during the on treatment period (median=77.5, IQR= 40-111, Table 35). After treatment completion, the highest median number of outpatient admissions among childhood survivors was for leukaemia (median=29, IQR=19-40), and among TYA survivors was for lymphoma (median=14, IQR=8-24). The median number of admissions during the treatment period was almost triple the rate of outpatient admissions after treatment completion among children, and it was double among TYAs with leukaemia.

Children had a higher median number of outpatient admissions than TYAs by almost the double during both the treatment phase (median=35 and 16, respectively) and after treatment completion (median=24 and 12, respectively).

The trends in the proportions of admissions by type of admissions (inpatient and outpatient) were analysed, from the year 2003 to 2010 (Figure 56), where the outpatient data were available for analysis. The trends in proportion of admissions by admission type were fairly steady from 2003 to 2010, and the ratio of inpatient to outpatient admissions was similar during this period, having a ratio of 1:3 admissions.

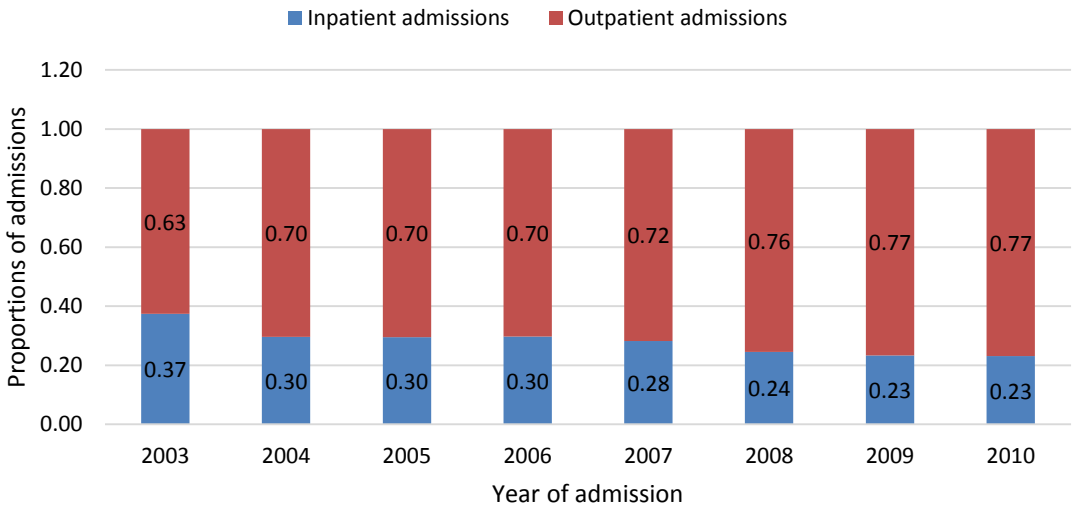


Figure 56: Trend of proportions of admissions 2003-2011 by type of admissions

Table 35:Median number and interquartile range of outpatient admission by period of admissions period by cancer types and age group

Cancer types ICCC-3	On treatment				Post-treatment				Overall			
	0-14		15-29		0-14		15-29		0-14		15-29	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Leukaemia	77.5	40-111	22.5	11-66	29	19-40	12	0-32	80	29-124	21	0-60
Lymphoma	21	14-37	18	10-29	19	13-31	14	8-24	31	19-47	24	12-39
CNS	28	11-49	16	8-30	29	12-47	6	0-20	37.5	18.5-66.5	15.5	0-35
Neuroblastoma	28	16-47	14	10-31.5	17	10-32	0	0-0	27	18-56	0	0-7
Renal tumours	25	13-45	16	8-24	17	12-23	2.5	0-22	33	16-56	3	0-25
Bone tumours	29	20-44	18	12-25	21	12-33	11	0-24	46	23-62	20.5	3-36
STS	22.5	13-36.5	16	6-31	22.5	11.5-48	5.5	0-16	31.5	15-61	11	0-28
Germ cell tumours	20	9-23	10	6-15	19	12-31	12	7-19	26.5	16-37	18	10-26
All cancers	35	16-67	16	9-30	24	14-38	12	3-21	39	20-79	19	7-34

Abbreviations: ICCC-3 = International Classifications of Cancer Type 3rd edition, CNS = central nervous tumours, STS = soft tissue sarcoma, IQR = interquartile range

6.4 Summary

The Cancer Forum in Australia identified cancer survivors as any cases diagnosed with cancer, and survivorship as starting from the date of diagnosis until a person reaches a balance in their life [202]. However, the focus of cancer epidemiological research was on long-term survivors who were disease-free for more than five years [17, 71, 72, 87]. This highlights the paucity of information on short-term survivors from the date of diagnosis, which limits the ability to provide those cases with optimal care, i.e. sufficient services designed to meet survivors' future needs. Consequently, the equity in accessing health services from the date of diagnosis has not been studied before, highlighting a significant literature gap in health services and quality of life among short-term survivors. Therefore, this chapter aimed to fill this gap by describing the patterns of admission from date of diagnosis; this was broken down into treatment period and post-treatment period. It was found that there were clear disproportions in admissions and length of stay in the two follow-up periods – on treatment and post-treatment – by age group at diagnosis, sex, ethnicity and deprivation, using the binary analysis adjusting for person-years and treatment duration by cancer type.

Children with bone tumours had higher hospital admissions and lengths of stay compared with other diagnostic groups, in both periods: on treatment and post-treatment. In addition, among TYA it was higher for cases with leukaemia and neuroblastoma. Females had higher rates of admission than males adjusting for person-years. Cases diagnosed with leukaemia had a higher number of BMTs than other diagnostic groups. Cases with bone tumours, neuroblastoma and leukaemia had higher percentages of relapses than other diagnostic groups. Therefore, these cancers are expected to have higher rates of admissions due to the cancer or its related treatment.

On average, children had higher numbers of admissions than TYAs during the study period. The number of admissions was four times higher during the treatment period than the post-treatment period. After adjusting for person-years, children had three times more admissions than TYAs. The difference in admissions between gender was minor, however South Asians had higher rates of admission, on average, compared with non-South Asians, except for those with STSs, and the difference was significant among cases diagnosed with bone tumours or STSs. The median rate of admission increased with increasing level of deprivation. Relapse cases had four times the rate of admissions than non-relapsed cases. The rate of admission and length of stay decreased during the follow-up period from date of diagnosis to the end of admission follow-up period. Children stayed longer in hospital compared with TYAs for all cancers combined, however TYAs

with leukaemia stayed longer than children during the on treatment phase. During the post-treatment phase, TYAs with neuroblastoma or renal tumours stayed longer than children. Outpatient admissions for children were higher among cases with leukaemia, and for TYAs were higher for cases diagnosed with lymphoma for females and germ cell tumours for males.

These results were based on binary analysis, hence the combination of demographics and clinical factors were not adjusted for in this chapter. Therefore, in Chapter 7, a multivariable analysis is adopted to quantify the hospital burden among the study population, taking into account population case mix. In addition, the hospital burden will be assessed in terms of type of cancer-related morbidity after completion of cancer treatment, in Chapter 8.

Chapter 7 Hospital Activity Rate Ratio

7.1 Introduction

Hospitalisation rate ratios (HRR) and Hospital days rate ratio (DRR) are presented in this chapter, based on multivariable modelling, to identify factors influencing patterns of admissions and lengths of stay for all cancers combined and by specific histological type (leukaemia, lymphoma, CNS, neuroblastoma, renal tumours, bone tumours, STS and germ cell tumours) (Aim 3, Question 4). In addition, this chapter includes a series of sensitivity analyses of the differences in hospital admissions between: 1) survivors and cases who died during the study period; 2) relapsed and non-relapsed cases; and 3) cases receiving a BMT compared to cases who did not receive a BMT.

One of the explanatory variables was the proportion of specialist care admissions. (More detail on how proportions of specialist care were identified can be found earlier in Section 4.11.6.) The amount of specialist care was estimated differently for each outcome. For the number of admissions, it was the total number of specialist admissions divided by the total number of admissions. While for the duration of admissions, it was the total number of bed days spent in specialist centre divided by total number of bed days spent in hospital.

7.2 Modelling

7.2.1 Inpatient hospital admissions

7.2.1.1 Model selection

A negative binomial regression model was significantly better than a Poisson model in describing the data for all diagnostic groups, based upon AIC and BIC (more detail in Section 4.12.3). The choice of variable form varied by diagnostic type. For example, leukaemia cases having age at diagnosis included in the model as a categorical term (0-14 vs 15-29) and year of diagnosis, deprivation score and proportion of specialist admission as continuous terms, proved a better fit model. Whilst for lymphoma cases the best model fit occurred when all explanatory variables were in continuous form.

Table 36: Explanatory variables and model fit assessment (AIC and BIC) by diagnostic group (ICCC-3)

Variables included in the model	Leukaemia N=615		Lymphoma N=635		CNS N=463		Neuroblastoma N=96	
	AIC	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**
Model selection (gender and age as continuous)								
Poisson	21678.88	21692.14	20648.77	20662.13	11110.38	11122.79	4319.58	4327.28
Negative binomial	**5965.61**	**5983.29**	**5593.57**	**5611.39**	**3537.29**	**3553.84**	**886.57**	**896.83**
Age variable (including gender)								
Continuous (by year 0-29)	5965.61	5983.29	**5593.57**	**5611.39**	3537.29	**3553.84**	886.57	896.83
Categorical (0-4,5-9, 10-14,15-19,20-24,25-29)	5969.09	6004.46	5598.15	5633.78	**3532.16**	3565.26	**883.10**	**903.61**
Categorical (0-14,15-29)	**5965.16**	**5982.85**	5598.59	5616.40	3564.78	3581.33	884.89	895.15
Year of diagnosis (gender, age, deprivation)								
Continuous (1996-2009)	**5919.07**	**5941.18**	**5557.36**	**5579.62**	**3520.00**	**3540.69**	**884.35**	**907.43**
Categorical (1996-1999, 2000-2004,2005-2009)	5929.29	5955.82	5560.47	5587.19	3523.47	3548.30	885.95	911.60
Deprivation score (gender and age)								
Continuous (least to most deprived)	**5920.80**	**5947.33**	**5558.68**	**5585.40**	**3517.38**	**3542.21**	**886.06**	**911.71**
Categorical (least deprived,2,3,4,most deprived)	5922.83	5962.62	5562.05	5602.13	3518.13	3555.37	889.86	923.20
Proportion of specialist care (age, gender, deprivation, year of diagnosis)								
Continuous	**5921.99**	**5952.94**	**5559.75**	**5590.92**	3506.75	**3535.71**	887.67	**915.88**
Categorical (limited specialist care <30%, some specialist care 30%-69%, mostly specialist care ⩾ 70%)	5922.83	5958.20	5560.37	5596.00	**3504.94**	3538.04	**886.98**	917.75
All variables								
Age, gender, year of admission, deprivation score, ethnicity, proportions of specialist care, relapsed and treatment type	5842.27	5908.59	5296.847	5368.11	3324.99	3391.20	835.64	884.36

Abbreviations: AIC = Akaike's information criterion and BIC = Bayesian information criterion
The variable between brackets is the variable included in the model

Table 37: Explanatory variables and model fit assessment (AIC and BIC) by diagnostic group (ICCC-3).

	Renal tumours N=92		Bone tumours N=150		STS N=252		Germ cell tumours N=564		Overall N =3,151	
Variables included in the model	**AIC**	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**
Model selection (gender and age as continuous)										
Poisson	2819.85	2827.41	4764.64	4773.67	10571.91	10582.5	7945.58	7958.59	106119.1	106137.3
Negative binomial	**796.80**	**806.89**	**1376.72**	**1388.77**	**2171.30**	**2185.42**	**3826.09**	**3879.43**	**27103.31**	**27127.53**
Age variable (including gender)										
Continuous (by year 0-29)	**796.80**	**806.89**	1376.72	**1388.77**	2171.30	**2185.42**	3862.09	3879.43	27103.31	**27127.53**
categorical (0-4,5-9, 10-14,15-19,20-24,25-29)	803.08	832.26	**1373.88**	1397.96	**2170.34**	2198.57	**3838.98**	**3873.66**	**27083.39**	27131.83
categorical (0-14,15-29)	797.11	807.20	1381.60	1393.65	2176.88	2191.00	3871.99	3889.33	27177.54	27201.76
Deprivation score (gender and age)										
Continuous (least to most deprived)	**797.68**	**810.29**	**1377.64**	**1392.70**	**2171.56**	**2189.21**	3833.66	**3872.67**	**27105.01**	**27135.29**
Categorical (least deprived, 2,3,4, most deprived)	804.11	824.28	1383.26	1407.34	2174.47	2202.71	**3829.85**	3881.87	27109.43	27157.88
Year of diagnosis (gender, age, deprivation)										
Continuous (1996-2009)	782.17	**797.30**	1379.797	1406.89	**2156.34**	**2177.52**	**3747.1**	**3790.45**	**26971.05**	**27007.38**
Categorical (1996-1999, 2000-2004,2005-2009)	**781.56**	799.22	**1372.49**	**1402.59**	2156.82	2181.53	3777.43	3825.11	26998.15	27040.54
Proportion of specialist care (age, gender, deprivation, year of diagnosis)										
Continues	**775.45**	**793.10**	**1360.05**	**1393.17**	2150.12	**2174.83**	3709.05	3756.73	26929.8	26972.19
categorical (limited specialist care <30%, some specialist care 30%-69%, mostly specialist care ⩾70%)	777.64	797.81	1362.29	1398.42	**2146.99**	2175.22	**3701.88**	**3753.90**	**26912.45**	**26960.89**
All variables										
Age, gender, year of admission, deprivation score, ethnicity, proportions of specialist care, relapsed and treatment type	754.72	787.51	1314.88	1378.10	1961.91	2018.38	3486.66	3577.70	25727.1	25830.04

Abbreviation: AIC = Akaike's information criterion and BIC = Bayesian information criterion
The variable between brackets is the variable included in the model

7.2.1.2 Estimation from the final model

The total number of inpatient admissions which occurred on or after the date of diagnosis for each patient was the dependent variable (outcome), and the number of person-years was considered as the exposure (follow-up person-years). Complete methodological details can be found in Section 4.12.3.

The study predictor variables (gender, age at diagnosis, year of diagnosis, proportion of specialist admission, ethnicity, deprivation, relapsed status and treatment type) were included based on their clinical importance. The pattern of admission could be affected by several variables, as explained in Chapter 3. For example, children may visit the hospital often during treatment due to the intensity of treatment, hence admissions due to treatment complications. Additionally, males with leukaemia have a longer treatment duration than females, consequently are more likely to have hospital visits than females. Furthermore, the clinical characteristics, such as type of initial treatment, might directly influence the pattern of hospital admissions. Patients receiving surgical interventions were likely to visit the hospital before the date of surgery for a routine check-up before the operation and may have follow-up visits for health status and post-operative care. Therefore, the entire demographic and clinical variables available in the datasets were included, even if they were not statistically significant.

The HRR was estimated, (i) overall for all cancers combined, and (ii) subdivided according to diagnostic group: leukaemia, lymphoma, CNS, neuroblastoma, renal tumours, bone tumours, STS and germ cell tumours.

7.2.1.2.1 Leukaemia

For leukaemia cases, there was no difference in the rate of admission and gender or age at diagnosis (Table 38). The rate of admission increased significantly by 10% (*P*-value <0.002) by each year increase in year of diagnosis. HRR of relapsed cases had double the rate of non-relapsed cases and was statistically significant. Cases with leukaemia treated with radiotherapy alone had a significantly lower HRR than cases treated with chemotherapy alone (HRR=0.26, 95%CI:0.10-0.68). While, cases treated with a combination of chemotherapy and radiotherapy or combination of chemotherapy and surgery had a greater HRR than cases treated with chemotherapy alone, after adjusting for person-years of 1.34 and 2.09 times higher admission rates, respectively.

Table 38: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for leukaemia (n= 615)

Characteristics	HRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.00	0.87 - 1.14	0.958
Age at diagnosis			
0-14	1 (ref)		
15-29	1.11	0.93-1.33	0.261
Year of diagnosis	1.10	1.08-1.12	<0.001
Deprivation*	1.01	0.99-1.03	0.409
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.10	0.85-1.42	0.495
Proportion of specialist care[¥]	1.15	0.94-1.42	0.285
Relapsed			
No	1 (ref)		
Yes	2.22	1.85-2.67	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.26	0.10-0.68	0.006
Surgery alone	1.07	0.22-5.32	0.930
Chemotherapy and radiotherapy	1.34	1.02-1.77	0.038
Chemotherapy and surgery	2.09	1.32-3.32	0.002
Radiotherapy and surgery	NA	NA	NA
Chemotherapy, radiotherapy and surgery	0.45	0.14-1.40	0.166
No recorded treatment	1.91	1.01-3.60	0.045

Abbreviations: HRR = hospital admission rate ratio; NA = not applicable i.e. there were no individuals; ref = reference category

[β] The hospital admission rate ratio was estimated adjusting for person-years at risk

* Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.1.2.2 Lymphoma

Among lymphoma cases, the HRR was not statistically different between gender and age (Table 39). However, there was a statistically significant increase in the rate of admission by 10% (95%CI: 8-13%) by year of diagnosis. Relapsed cases had four-times significantly higher rate of admission than cases with no relapse. The rate of admission by initial treatment type was significantly lower among cases treated with radiotherapy alone, surgery alone or radiotherapy and surgery than cases treated with chemotherapy alone by 88%, 76% and 80%, respectively.

Table 39: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for lymphoma (n=635)

Characteristics	**HRR**[β]	**95% CI**	***P*-value**
Gender			
Male	1 (ref)		
Female	1.03	0.89-1.20	0.659
Age at diagnosis	1.00	0.99-1.01	0.970
Year of diagnosis	1.10	1.08-1.13	<0.001
Deprivation*	1.00	0.97-1.02	0.866
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.17	0.89-1.53	0.255
Proportion of specialist care[¥]	1.07	0.87-1.30	0.540
Relapsed			
No	1 (ref)		
Yes	4.11	3.27-5.18	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.11	0.07-0.17	<0.001
Surgery alone	0.24	0.14-0.42	<0.001
Chemotherapy and radiotherapy	0.91	0.72-1.15	0.426
Chemotherapy and surgery	0.78	0.61-1.00	0.049
Radiotherapy and surgery	0.20	0.11-0.36	<0.001
Chemotherapy, radiotherapy and surgery	0.96	0.59-1.56	0.866
No recorded treatment	0.29	0.17-0.49	<0.001

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

β The hospital admission rate ratio was estimated adjusting for person-years at risk

* Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

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7.2.1.2.3 Central nervous system (CNS) tumours

The rate of hospitalisation decreased significantly by 3% with age among cases with CNS tumours (Table 40). There was a 4% significant increase in the rate of admission by year of diagnosis. The rate of admission was higher among cases living in the most deprived areas compared with cases living in the least deprived areas (24%, 95% CI:6%-45% cases with deprivation scores on the 75th percentile compared to those on the 25th percentile, data not shown), this agreed with the pattern of admission and deprivation in the univariable analysis in Section 6.2.1.7.4. Relapsed CNS cases had almost double the rate of admission per person-year compared with non-relapsed cases and was significant (P-value <0.001). Cases treated with radiotherapy alone, surgery alone, radiotherapy and surgery, or with no recorded treatment had significantly lower rates of admission than cases treated with chemotherapy alone by 63%, 72%, 67% and 79% respectively.

Table 40: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for central nervous system (CNS) (n=463)

Characteristics	**HRR$^{\beta}$**	**95% CI**	***P*-value**
Gender			
Male	1 (ref)		
Female	0.99	0.82-1.19	0.903
Age at diagnosis	0.97	0.96-0.98	<0.001
Year of diagnosis	1.04	1.02-1.07	0.001
Deprivation*	1.04	1.01-1.07	0.006
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.00	0.68-1.48	0.985
Proportion of specialist care¥	1.25	0.97-1.61	0.080
Relapsed			
No	1 (ref)		
Yes	1.93	1.49-2.50	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.37	0.22-0.61	<0.001
Surgery alone	0.28	0.20-0.38	<0.001
Chemotherapy and radiotherapy	1.15	0.75-1.77	0.528
Chemotherapy and surgery	1.25	0.85-1.85	0.253
Radiotherapy and surgery	0.33	0.21-0.52	<0.001
Chemotherapy, radiotherapy and surgery	0.94	0.64-1.37	0.728
No recorded treatment	0.21	0.15-0.30	<0.001

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

$^{\beta}$The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.1.2.4 Neuroblastoma

Females with neuroblastoma had fewer hospital admissions than males by 14% (95%CI:0.57-1.30), but this was not statistically significant (Table 41). Neuroblastoma treated with radiotherapy alone or radiotherapy and surgery showed a significantly lower rate of admission than cases with chemotherapy alone by 95% and 97%, respectively. Cases with no treatment had a 92% significant lower rate of admission than cases treated with chemotherapy only.

Table 41: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for neuroblastoma (n=96)

Characteristics	**HRR$^{\beta}$**	**95% CI**	***P*-value**
Gender			
Male	11 (ref)		
Female	0.86	0.57-1.30	0.475
Age at diagnosis			
0-4	1 (ref)		
5-9	1.34	0.76-2.38	0.316
10-14	0.52	0.15-1.85	0.313
15-19	0.28	0.06-1.24	0.093
20-24	4.53	0.53-38.95	0.169
25-29	2.60	0.95-7.14	0.064
Year of diagnosis	1.03	0.97-1.09	0.353
Deprivation	0.99	0.93-1.06	0.745
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.89	0.34-2.35	0.816
Proportion of specialist care	0.91	0.43-1.91	0.796
Relapsed			
No	1 (ref)		
Yes	1.35	0.82-2.22	0.235
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	NA	NA	
Surgery alone	0.05	0.03-0.09	<0.001
Chemotherapy and radiotherapy	0.47	0.19-1.14	0.096
Chemotherapy and surgery	0.75	0.45-1.24	0.256
Radiotherapy and surgery	0.03	0.00-0.57	0.020
Chemotherapy, radiotherapy and surgery	0.72	0.26-1.94	0.511
No recorded treatment	0.08	0.03-0.24	<0.001

Abbreviations: HRR = hospital admission rate ratio; NA = not applicable i.e. there were no individuals in this category; ref = reference category

$^{\beta}$The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.1.2.5 Renal tumours

Cases with renal tumours showed a 4%, 95%CI: 1-7% increase in the rate of admission for every single year increase in age, and a significant 14%, 95% CI:7-21% (Table 42) increase in admission for each increase in year of diagnosis, i.e. cases diagnosed recently had higher rates of admission. There was a significant increase in the rate of admission among cases with all of their admissions in specialist care, compared with cases with no specialist admissions. Cases with proportion of specialist score on the 75th percentile (100% of admissions was in specialist centre) had 1.66-times higher rate of admissions than cases on the 25th percentile (45% of their admissions was in specialist centre) (95%CI:1.16-2.36, data not shown). Relapsed cases with renal tumours had three-fold the rate of admission than cases with no relapse and this effect was significant. Cases with surgery alone had 68% lower rate of admission compared with cases treated with chemotherapy alone and was statistically significant.

Table 42: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for renal tumour (n=92)

Characteristics	**HRR$^{\beta}$**	**95% CI**	***P*-value**
Gender			
Male	1 (ref)		
Female	1.02	0.66-1.59	0.934
Age at diagnosis	1.04	1.01-1.07	0.005
Year of diagnosis	1.14	1.07-1.21	<0.001
Deprivation	0.99	0.93-1.06	0.792
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.72	0.31-1.69	0.452
Proportion of specialist care	2.65	1.34-5.22	0.005
Relapsed			
No	1 (ref)		
Yes	3.69	1.82-7.48	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	NA	NA	
Surgery alone	0.32	0.16-0.65	0.001
Chemotherapy and radiotherapy	1.63	0.36-7.31	0.524
Chemotherapy and surgery	0.81	0.49-1.34	0.408
Radiotherapy and surgery	NA	NA	
Chemotherapy, radiotherapy and surgery	0.70	0.25-1.97	0.495
No recorded treatment	NA	NA	

Abbreviations: HRR = hospital admission rate ratio; NA = not applicable i.e. there were no individuals in this category; ref = reference category.

$^{\beta}$the hospital admission rate ratio was estimated adjusting for person-years at risk

*deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.1.2.6 Bone tumours

The rate of admission among bone tumour cases decreased for every single year increase in age by 3% and was statistically significant (95%CI:1%-5%) (Table 43). The rate of admission was significantly higher among cases diagnosed in later study periods; HRR was almost double in 2000-2004 than in 1996-1999 and in 2005-2009. Relapsed cases had a significantly increased rate of admissions than non-relapsed cases. Cases with radiotherapy alone or surgery alone had 85% and 81% lower rates of admission than cases treated only with chemotherapy. Cases with no treatment were 92% less likely to be admitted than cases treated with chemotherapy only.

Table 43:Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for bone tumours (n=150)

Characteristics	HRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.21	0.89-1.64	0.222
Age at diagnosis	0.97	0.95-0.99	0.015
Year of diagnosis			
1996-1999	1 (ref)		
2000-2004	1.95	1.20-2.91	0.006
2005-2009	2.31	1.34-2.94	0.001
Deprivation			
Most deprived	1 (ref)		
2	0.98	0.43-1.09	0.107
3	0.99	0.51-1.21	0.271
4	0.89	0.49-1.31	0.369
Least deprived	1.29	0.58-1.48	0.755
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.80	0.47-1.87	0.864
Proportion of specialist care			
Mostly specialist admission	1 (ref)		
Some specialist admission	0.67	0.39-1.20	0.186
Limited specialist admission	1.00	0.57-1.52	0.788
Relapsed			
No	1 (ref)		
Yes	1.79	1.23-2.43	0.005
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.16	0.04-0.64	0.010
Surgery alone	0.18	0.10-0.33	<0.001
Chemotherapy and radiotherapy	0.86	0.44-1.66	0.643
Chemotherapy and surgery	0.88	0.63-1.24	0.481
Radiotherapy and surgery	0.13	0.04-0.46	0.002
Chemotherapy, radiotherapy and surgery	0.89	0.37-2.13	0.792
No recorded treatment	0.07	0.03-0.16	<0.001

Abbreviations: HRR-Hospital admission rate ratio; ref-reference category. [β]the hospital admission rate ratio was estimated adjusting for person-years at risk .*deprivation criteria was classified using Townsend score.

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.1.2.7 Soft tissue sarcoma (STS)

Cases with STS had an 11% increase in the rate of admissions for each single year increase in diagnosis year. South Asians diagnosed with STS had significantly lower rates of admission than non-South Asians (HRR= 0.58, 95%CI: 0.36-0.95) (Table 44). Relapsed cases had double the rate of admission than non-relapsed cases and this was statistically significant. Cases treated with radiotherapy alone, surgery alone, a combination of radiotherapy and surgery, or had no record of treatment had significant lower rates of admissions compared with cases treated with chemotherapy alone by 92%, 94%, 95% and 84%, respectively.

Table 44: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for soft tissue sarcoma (STS) (n=252)

Characteristics	**HRR$^{\beta}$**	**95% CI**	***P*-value**
Gender			
Male	1 (ref)		
Female	1.09	0.83-1.43	0.518
Age at diagnosis	1.00	0.99-1.02	0.540
Year of diagnosis	1.11	1.07-1.15	<0.001
Deprivation	0.97	0.94-1.01	0.159
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.58	0.36-0.95	0.032
Proportion of specialist care¥	0.79	0.53-1.18	0.252
Relapsed			
No	1 (ref)		
Yes	2.09	1.47-2.98	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.08	0.03-0.27	<0.001
Surgery alone	0.06	0.04-0.09	<0.001
Chemotherapy and radiotherapy	0.86	0.57-1.29	0.459
Chemotherapy and surgery	1.08	0.73-1.60	0.684
Radiotherapy and surgery	0.05	0.02-0.13	<0.001
Chemotherapy, radiotherapy and surgery	0.59	0.31-1.10	0.097
No recorded treatment	0.16	0.08-0.30	<0.001

Abbreviations**:** HRR = hospital admission rate ratio; ref = reference category

$^{\beta}$the hospital admission rate ratio was estimated adjusting for person-years at risk

*deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.1.2.8 Germ cell tumours

Females with germ cell tumours had a 27% higher rate of admissions compared with males in the univariable analysis, and it was consistent in the multivariable analysis after adjusting for other social and clinical variables (Table 45). Children aged 5-9 years at diagnosis had a lower rate of admission compared with younger children aged 0-4 at diagnosis, with a difference of 46%. Similarly, TYAs aged 20-24 and 25-29 had lower rates of admission compared with children aged 0-4 years at diagnosis (HRR= 44% and 57%, respectively). In addition, the rate of admission increased significantly for each increase in single year of diagnosis by 12%. Cases receiving limited specialist care had significantly lower rates of admission than cases receiving mostly specialist care, with differences of 24%. Relapsed cases has almost double the rate of admissions than cases with no relapses, which was a significant effect. Cases treated with radiotherapy alone, surgery alone, chemotherapy and surgery, radiotherapy and surgery, a combination of all, or had no recorded treatment had significant lower rates of admission than cases treated only with chemotherapy by 92%, 88%, 55%, 82% and 89%, respectively.

Table 45: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for germ cell tumours (n=564)

Characteristics	HRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.27	0.99-1.63	0.058
Age at diagnosis			
0-4	1 (ref)		
5-9	0.36	0.17-0.78	0.009
10-14	0.66	0.38-1.14	0.136
15-19	0.68	0.44-1.05	0.082
20-24	0.56	0.37-0.84	0.006
25-29	0.43	0.29-0.64	<0.001
Year of diagnosis	1.12	1.10-1.15	<0.001
Deprivation	1.03	1.00-1.05	0.059
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.04	0.75-1.46	0.799
Proportion of specialist care			
Mostly specialist admission	1 (ref)		
Some specialist admission	1.11	0.85-1.45	0.444
Limited specialist admission	0.76	0.61-0.93	0.008
Relapsed			
No	1 (ref)		
Yes	1.90	1.34-2.71	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.08	0.02-0.35	0.001
Surgery alone	0.12	0.09-0.18	<0.001
Chemotherapy and radiotherapy	1.45	0.58-3.61	0.428
Chemotherapy and surgery	0.45	0.33-0.63	<0.001
Radiotherapy and surgery	0.14	0.10-0.21	<0.001
Chemotherapy, radiotherapy and surgery	0.88	0.42-1.09	0.739
No recorded treatment	0.11	0.05-0.22	<0.001

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

[β]The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.1.2.9 Overall cancers

For all cancers combined, there were no differences in gender and rate of admission. However, the rate of admission decreased with every single year increase in age by 2%. There was an 8% increase in the rate of admission for every single year increase in year of diagnosis, a significant change. There was a significant increase in the admission by 8% (95% CI:2%-15%,*P*-value=0.011) among individuals with deprivation score on the 75th percentile compared with those on the 25th, data not shown. The rate of admission was 29% and 21% lower per person-year among cases receiving some and limited specialist care, respectively, compared with cases receiving mostly specialist care, with a significant effect (Table 46). Relapsed cases had significantly more than double the rate of admissions than non-relapsed case. Cases treated with a combination of chemotherapy and radiotherapy had a significant higher rate of admission, by 18% compared to cases treated with chemotherapy alone. While all other treatment regimes, whether single or complex modalities, had a lower rate of admission than cases treated with chemotherapy alone; which was statistically significant.

Table 46: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for all cancers combined (n=3,151)

Characteristics	HRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.05	0.97-1.13	0.230
Age at diagnosis	0.98	0.98-0.98	<0.001
Year of diagnosis	1.08	1.07-1.09	<0.001
Deprivation	1.02	1.00-1.03	0.011
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.91	0.79-1.05	0.200
Proportion of specialist care			
Mostly specialist admission	1 (ref)		
Some specialist admission	0.71	0.63-0.81	<0.001
Limited specialist admission	0.79	0.72-0.87	<0.001
Relapsed			
No	1 (ref)		
Yes	2.63	2.35-2.93	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.19	0.14-0.26	<0.001
Surgery alone	0.17	0.15-0.19	<0.001
Chemotherapy and radiotherapy	1.18	1.01-1.37	0.036
Chemotherapy and surgery	0.69	0.62-0.77	<0.001
Radiotherapy and surgery	0.14	0.12-0.17	<0.001
Chemotherapy, radiotherapy and surgery	0.77	0.62-0.95	0.014
No recorded treatment	0.52	0.46-0.59	<0.001

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

[β]The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.2 Number of days in hospital rate ratio (DRR)

7.2.2.1 Model selection

The choice of the variable form for the length of stay analysis was similar to the hospital admission rate ratio, and was based on the BIC and AIC criteria (Table 47). The choice of the variable form varied by diagnostic group, whilst each diagnostic group was modelled separately. Negative binomial regression had a better fit than the Poisson regression model.

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Table 47: Explanatory variables and model fit assessment(AIC and BIC) criteria by diagnostic group (ICCC-3)

Variables included in the model	Leukaemia N=615		Lymphoma N=635		CNS N=463		Neuroblastoma N=96	
	AIC	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**
Model selection (gender and age as continuous)								
Poisson	91379.9	91393.11	71037.78	71051.14	42146.1	42158.5	15522.3	15529.98
Negative binomial	**7748.44**	**7766.13**	**6920.37**	**6938.18**	**4791.87**	**4808.42**	**1132.88**	**1143.17**
Age variable (including gender)								
Continuous (by year 0-29)	7748.44	7766.13	6920.37	**6938.18**	4791.87	**4808.42**	1132.88	**1143.17**
Categorical (0-4,5-9, 10-14,15-19,20-24,25-29)	7733.81	7769.18	**6919.33**	6954.96	**4787.95**	4821.05	**1129.32**	1149.83
Categorical (0-14,15-29)	**7729.19**	**7746.88**	6932.17	6949.98	4794.46	4811.01	1133.62	1143.87
Year of diagnosis (gender, age, deprivation)								
Continuous (1996-2009)	7729.17	**7751.28**	6920.54	**6942.81**	**4787.45**	**4808.14**	**1133.25**	**1146.07**
Categorical (1996-1999, 2000-2004,2005-2009)	**7727.43**	7753.96	**6918.98**	6945.71	4787.94	4812.77	1135.87	1151.26
Deprivation score (gender and age)								
Continuous (least to most deprived)	7730.64	**7757.17**	6922.41	**6949.13**	**4764.01**	**4788.83**	**1134.06**	**1149.45**
Categorical (least deprived, 2,3,4, most deprived)	**7722.14**	7761.93	**6920.42**	6960.50	4775.40	4812.64	1134.24	1157.32
Proportion of specialist care (age, gender, deprivation, year of diagnosis)								
Continues	**7732.62**	**7763.57**	**6892.09**	**6923.27**	4766.01	**4794.97**	1135.84	**1153.79**
Categorical (limited specialist care <30%, some specialist care 30%-69%, mostly specialist care ⩾70%)	7734.16	7769.53	6901.36	6936.99	**4762.64**	4795.74	**1133.32**	1153.83
All variables								
(age, gender, year of admission, deprivation score, ethnicity, proportions of specialist care, relapsed and treatment type)	7649.63	7720.38	6724.60	6795.86	4725.99	4792.19	1125.58	1164.04

Abbreviations: AIC = Akaike's information criterion and BIC = Bayesian information criterion

The variable between brackets is the variable included in the model

Table 48: Explanatory variables and model fit assessment (AIC and BIC) criteria by diagnostic group (ICCC-3)

Variables included in the model	Renal tumours N=92		Bone tumours N=150		STS N=252		Germ cells tumours N=564		Overall N =3,151	
	AIC	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**	**AIC**	**BIC**
Model selection (gender and age as continuous)										
Poisson	9832.6	9840.2	23002.15	23011.19	37517.13	37527.72	33505.47	33518.5	420669.	420687.6
Negative binomial	**1004.8**	**1014.9**	**1855.30**	**1867.34**	**2837.17**	**2851.28**	**5170.34**	**5187.7**	**35081.5**	**35105.74**
Age variable (including gender)										
Continuous (by year 0-29)	**1004.8**	**1014.9**	1855.30	**1867.34**	**2837.17**	**2851.28**	5170.34	**5187.7**	35081.5	35105.74
categorical (0-4,5-9, 10-14,15-19,20-24,25-29)	1010.5	1030.7	**1849.37**	1873.46	2841.66	2869.90	**5163.13**	5197.8	**35055.5**	**35103.97**
categorical (0-14,15-29)	1004.9	1015.0	1859.08	1871.13	2839.04	2853.15	5173.59	5190.9	35116.4	35140.60
Deprivation score (gender and age)										
Continuous (least to most deprived)	**1005.8**	**1018.4**	**1856.83**	**1871.88**	**2838.60**	**2856.24**	5156.19	5177.9	**35053.5**	**35107.97**
Categorical (Least deprived,2,3,4,Most deprived)	1007.1	1027.3	1862.28	1886.37	2843.44	2871.68	**5141.7**	**5176.4**	35053.1	35126.37
Year of diagnosis (gender, age, deprivation)										
Continuous (1996-2009)	1006.1	**1021.2**	1852.49	1870.56	**2837.81**	**2858.98**	**5114.50**	**5153.52**	**35034.6**	**35095.2**
Categorical (1996-1999, 2000-2004,2005-2009)	**1006.0**	1023.7	**1849.29**	**1870.36**	2838.80	2863.51	5134.74	5178.09	35043.5	35110.2
Proportion of specialist care (age, gender, deprivation, year of diagnosis)										
Continuous	**1000.7**	**1018.3**	**1843.09**	**1867.17**	**2833.10**	**2857.80**	5114.37	**5157.72**	**35013.1**	**35079.7**
categorical (limited specialist care <30%, some specialist care 30%-69%, mostly specialist care ⩾ 70%)	1002.1	1027.3	1847.23	1874.32	2835.03	2863.26	**5110.49**	5158.17	35024.5	35097.2
All variables (age, gender, year of admission, deprivation score, ethnicity, proportions of specialist care, relapsed and treatment type)	1000.7	1033.5	1784.19	1838.38	2722.40	2778.87	4978.01	5060.37	**34493.2**	**34614.3**

Abbreviations: AIC = Akaike's information criterion and BIC = Bayesian information criterion.The variable between brackets is the variable included in the model

7.2.2.2 Estimations from the final model

7.2.2.2.1 Leukaemia

Females diagnosed with leukaemia at the age of 0-29 had 19% more hospital days than males per person-day at risk, but was not statistically significant (Table 49). TYAs aged 15-29 at diagnosis had 2.27-fold longer stays per bed-day per person than children aged 0-14 at diagnosis, a significant effect. Cases with AML stayed longer by 96% compared with ALL (data not shown). Patients receiving limited specialist day care, had longer stays than cases receiving the majority of their hospital stays in a specialist unit, but this was not significant. Relapsed cases had 2.5-fold significantly longer stays in hospital than non-relapsed cases. Cases treated with radiotherapy alone had significant 80% shorter hospital stays than cases treated with chemotherapy alone, while cases treated with chemotherapy and surgery had 2.27-times longer hospital stays than cases treated with chemotherapy alone.

Table 49: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for leukaemia cases (n=615)

Characteristics	DRR$^{\beta}$	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.19	1.01-1.42	0.043
Age at diagnosis			
0-14	1 (ref)		
15-29	2.27	1.82-2.84	<0.001
Year of diagnosis	1.05	1.02-1.07	<0.001
Deprivation*	1.01	0.99-1.04	0.298
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.09	0.81-1.49	0.561
Proportion of specialist care¥	0.96	0.73-1.27	0.794
Relapsed			
No	1 (ref)		
Yes	2.50	1.99-3.14	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.20	0.06-0.67	0.008
Surgery alone	0.58	0.08-4.35	0.595
Chemotherapy and radiotherapy	1.05	0.75-1.47	0.762
Chemotherapy and surgery	2.27	1.29-3.99	0.004
Radiotherapy and surgery	NA		
Chemotherapy, radiotherapy and surgery	0.35	0.08-1.45	0.146
No recorded treatment	4.07	2.28-7.28	<0.001

Abbreviations: DRR = number of days in hospital rate ratio; ref = reference category

$^{\beta}$The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$

7.2.2.2.2 Lymphoma

Among cases with lymphoma aged 0-29 at diagnosis, there was a 4% increase in number of days for each single year increase in year of diagnosis (95% CI:1-7%:*P*-value=0.011). Cases who received a higher proportion of specialist care had significantly longer hospital stays than cases with limited specialist day care (DRR=2.22, 95%CI:1.69-2.91). Relapsed lymphoma cases had 4.25-times significantly longer stays than non-relapsed individuals. Cases treated with radiotherapy alone, surgery alone, radiotherapy and surgery, or a combination of all had shorter hospital stays than cases treated with chemotherapy alone by 94%, 86%, 87% and 55%, respectively.

Table 50: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for lymphoma cases (n=635)

Characteristics	**DRR[β]**	**95% CI**	***P*-value**
Gender			
Male	1 (ref)		
Female	0.87	0.71-1.07	0.181
Age at diagnosis	1.00	0.99-1.02	0.883
Year of diagnosis	1.04	1.01-1.07	0.011
Deprivation*	0.99	0.96-1.02	0.542
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.24	0.86-1.78	0.253
Proportion of specialist care[¥]	2.22	1.69-2.91	<0.001
Relapsed			
No	1 (ref)		
Yes	4.25	3.09-5.83	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.06	0.03-0.10	<0.001
Surgery alone	0.14	0.03-0.10	<0.001
Chemotherapy and radiotherapy	0.91	0.07-0.30	0.548
Chemotherapy and surgery	1.23	0.67-1.24	0.214
Radiotherapy and surgery	0.13	0.06-0.27	<0.001
Chemotherapy, radiotherapy and surgery	0.45	0.23-0.88	0.020
No recorded treatment	1.35	0.59-3.07	0.477

Abbreviations: DRR = number of days in hospital rate ratio; ref = reference category

[β]The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

$$¥\text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$$

7.2.2.2.3 Central nervous system (CNS) tumours

Females diagnosed with CNS tumours had significantly shorter stays than males (28%, 95%CI: 5-45%). The rate of stays increased significantly by year of diagnosis by 8% per person-day at risk. The rate of hospital days increased significantly with levels of deprivation, i.e cases with deprivation score on the 75th percentile had 1.77-fold longer stay than those on the 25th percentile (95%CI:1.43-2.19, *P*-value=<0.001), data not shown. CNS tumours had significantly shorter stays with increased levels of care received in specialist centre (DRR=0.69, 95%CI:0.48-0.98). Relapsed cases had 1.9-times significantly longer stays than non-relapsed cases. Cases treated with surgery alone had shorter hospital stays, by 47%, than cases treated with chemotherapy alone (Table 51). Additionally, cases showing no record of treatment had 56% shorter hospital stays than cases with chemotherapy alone.

Table 51: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for central nervous system cases (n=463)

Characteristics	DRR$^{\beta}$	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	0.72	0.55-0.95	0.018
Age at diagnosis	1.00	0.98-1.01	0.676
Year of diagnosis	1.08	1.04-1.12	<0.001
Deprivation*	1.12	1.07-1.16	<0.001
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.16	0.65-2.04	0.618
Proportion of specialist care¥	0.69	0.48-0.98	0.040
Relapsed			
No	1 (ref)		
Yes	1.90	1.29-2.80	0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.66	0.33-1.32	0.245
Surgery alone	0.53	0.32-0.85	0.009
Chemotherapy and radiotherapy	1.53	0.82-2.87	0.185
Chemotherapy and surgery	1.52	0.86-2.69	0.153
Radiotherapy and surgery	0.83	0.41-1.65	0.589
Chemotherapy, radiotherapy and surgery	0.93	0.53-1.64	0.813
No recorded treatment	0.44	0.26-0.73	0.002

Abbreviations: DRR = number of days in hospital rate ratio; ref = reference category

$^{\beta}$The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$

7.2.2.2.4 Neuroblastoma

There were no statistical differences among neuroblastoma cases in terms of hospital stays, except for cases treated initially with surgery alone, as they had 92% (95%CI:70-97%) shorter hospital stays than cases treated with chemotherapy alone

Table 52: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for neuroblastoma cases (n=96)

Characteristics	DRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.40	0.72-2.73	0.316
Age at diagnosis	0.97	0.93-1.01	0.208
Year of diagnosis	1.04	0.94-1.15	0.475
Deprivation*	1.06	0.96-1.17	0.286
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.65	0.14-3.00	0.586
Proportion of specialist care[¥]	1.13	0.38-3.35	0.822
Relapsed			
No	1 (ref)		
Yes	1.18	0.58-2.43	0.647
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	NA	NA	
Surgery alone	0.08	0.03-0.23	<0.001
Chemotherapy and radiotherapy	0.41	0.11-1.54	0.189
Chemotherapy and surgery	0.83	0.40-1.73	0.623
Radiotherapy and surgery	0.13	0.01-2.11	0.150
Chemotherapy, radiotherapy and surgery	0.53	0.12-2.38	0.407
No recorded treatment	1.63	0.45-5.89	0.457

Abbreviations: DRR = number of days in hospital rate ratio; NA = not applicable i.e. there were no individuals in this category; ref = reference category

[β]The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$

7.2.2.2.5 Renal tumours

Similar to neuroblastoma there were no statistical differences in terms of patient characteristics and hospital stay among renal tumour cases, except for the proportion of care in specialist units. Cases with proportion of specialist care on the 75th percentile (100% of their hospital stay was in specialist unit) had 2.26-times longer stay than cases on the 25th percentile (95%CI: 1.42-3.59, 48% of their stay was in specialist unit), data not shown.

Table 53: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for renal tumour cases (n=92)

Characteristics	DRR$^{\beta}$	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.24	0.64-2.42	0.524
Age at diagnosis	1.03	0.99-1.08	0.117
Year of diagnosis	1.05	0.96-1.14	0.269
Deprivation*	0.97	0.89-1.07	0.604
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.76	0.20-2.84	0.679
Proportion of specialist care¥	4.82	1.98-11.78	0.001
Relapsed			
No	1 (ref)		
Yes	2.28	0.80-6.48	0.123
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	NA	NA	
Surgery alone	0.71	0.26-1.95	0.511
Chemotherapy and radiotherapy	1.66	0.19-14.87	0.649
Chemotherapy and surgery	1.91	0.94-3.86	0.073
Radiotherapy and surgery	NA	NA	
Chemotherapy, radiotherapy and surgery	0.58	0.13-2.62	0.479
No recorded treatment	NA	NA	

Abbreviations: DRR = number of days in hospital rate ratio; NA = not applicable i.e. there were no individuals in this category; ref = reference category

$^{\beta}$The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

¥$\text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$

7.2.2.2.6 Bone tumours

The rate of hospital stays decreased by single increase in age by 2%, and increased by year of diagnosis, but was not significant. While, it was significantly higher among cases diagnosed during 2005-2009, as they had two-fold longer stays than cases diagnosed in 1996-1999. Relapsed cases had 1.68-times longer stays than non-relapsed cases and this effect was significant. Cases treated with radiotherapy alone, surgery alone, a combination of radiotherapy and surgery, or had no record of treatment had shorter hospital stays than cases treated with chemotherapy alone by 96%, 89%, 93% and 97%, respectively.

Table 54: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for bone tumour cases (n=150)

Characteristics	DRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.17	0.84-1.65	0.350
Age at diagnosis	0.98	0.96-1.01	0.208
Year of diagnosis			
1996-1999	1 (ref)		
2000-2004	1.61	0.99-2.62	0.054
2005-2009	2.35	1.51-3.66	<0.001
Deprivation*	1.05	1.00-1.11	0.057
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	1.14	0.54-2.43	0.725
Proportion of specialist care[¥]			
Mostly specialist intake	1 (ref)		
Some specialist intake	0.98	0.46-2.08	0.948
Limited specialist intake	1.15	0.69-1.90	0.596
Relapsed			
No	1 (ref)		
Yes	1.68	1.15-2.44	0.007
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.04	0.01-0.17	<0.001
Surgery alone	0.11	0.06-0.19	<0.001
Chemotherapy and radiotherapy	0.52	0.26-1.05	0.069
Chemotherapy and surgery	0.81	0.56-1.18	0.275
Radiotherapy and surgery	0.07	0.02-0.28	<0.001
Chemotherapy, radiotherapy and surgery	0.74	0.28-1.96	0.545
No recorded treatment	0.03	0.01-0.07	<0.001

Abbreviations: DRR= number of days in hospital rate ratio; ref = reference category

[β]The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

¥$\text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$

7.2.2.2.7 Soft tissue sarcoma (STS)

The rate of hospital days increased by each single year increase in age at diagnosis by 3% per person-days (Table 55). South Asians had 61% fewer hospital days than non-South Asians, which was significant (95%CI:29-78%, *P*-value=0.002). Cases receive with proportion of specialist care on the 75th percentile (100% of their hospital stay was in specialist unit) had 1.57 times longer stay than those on the 25th percentile 95%CI:1.20-2.06 (40% of their stay was in specialist unit, data not shown). Cases treated with radiotherapy alone, surgery alone and a combination of radiotherapy and surgery had shorter hospital stays than cases treated initially with chemotherapy alone by 92%, 25% and 95%, respectively.

Table 55: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for soft tissue sarcoma cases (n=252)

Characteristics	DRR$^{\beta}$	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.20	0.85-1.68	0.306
Age at diagnosis	1.03	1.01-1.05	0.010
Year of diagnosis	1.01	0.97-1.06	0.576
Deprivation*	0.98	0.94-1.03	0.459
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.39	0.22-0.71	0.002
Proportion of specialist care¥	2.13	1.36-3.35	0.001
Relapsed			
No	1 (ref)		
Yes	1.10	0.70-1.74	0.679
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.08	0.02-0.33	<0.001
Surgery alone	0.75	0.05-0.12	<0.001
Chemotherapy and radiotherapy	0.76	0.45-1.29	0.313
Chemotherapy and surgery	1.05	0.63-1.76	0.840
Radiotherapy and surgery	0.05	0.01-0.15	<0.001
Chemotherapy, radiotherapy and surgery	0.73	0.32-1.66	0.457
No recorded treatment	0.51	0.26-1.01	0.053

Abbreviations: DRR = number of days in hospital rate ratio; ref = reference category
$^{\beta}$The number of days in hospital rate ratio was estimated adjusting for person-days at risk
*Deprivation criteria was classified using Townsend score

$$¥\text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$$

7.2.2.2.8 Germ cell tumours

The rate of hospital days decreased significantly by 3% for every single year increase in age at diagnosis among germ cell tumour survivors (Table 56). The rate of hospital stays increased significantly by 13% for every single year increase in year of diagnosis. The rate of hospital stays were shorter as deprivation level decreased, and it was statistically significant among cases living in the least deprived group compared to those living in the most deprived areas. Patients who lived in the least deprived areas had 50% shorter stays than cases who lived in the most deprived areas. Relapsed cases had three-fold the rate of stay compared to non-relapsed cases, with a highly significant effect. Cases initially treated with radiotherapy alone, surgery alone, a combination of chemotherapy and surgery, a combination of radiotherapy and surgery, a combination of all, or no record of treatment, had significantly shorter hospital stays than cases with chemotherapy alone, having 96%, 87%, 60%, 91% and 93%, respectively. Although not significant, survivors treated with a combination of chemotherapy and radiotherapy stayed longer than survivors having chemotherapy alone (DRR= 2.14, 95%CI:0.60-7.60).

Table 56: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for germ cell tumour cases (n=564)

Characteristics	DRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	0.92	0.65-1.30	0.639
Age at diagnosis	0.97	0.96-0.99	0.008
Year of diagnosis	1.13	1.10-1.17	<0.001
Deprivation*			
Most deprived	1 (ref)		
2	0.72	0.49-1.04	0.083
3	0.44	0.31-0.63	0.000
4	0.97	0.66-1.42	0.874
Least deprived	0.50	0.34-0.75	<0.001
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.77	0.48-1.23	0.271
Proportion of specialist care[¥]	0.65	0.47-0.90	0.009
Relapsed			
No	1 (ref)		
Yes	3.00	1.76-5.12	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.04	0.00-0.29	0.002
Surgery alone	0.13	0.08-0.22	<0.001
Chemotherapy and radiotherapy	2.14	0.60-7.60	0.239
Chemotherapy and surgery	0.40	0.26-0.64	<0.001
Radiotherapy and surgery	0.09	0.05-0.16	<0.001
Chemotherapy, radiotherapy and surgery	0.73	0.24-2.22	0.584
No recorded treatment	0.07	0.03-0.18	<0.001

Abbreviations: DRR = number of days in hospital rate ratio; ref = reference category

[β]The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

$$¥\ \text{Amount of specialist care} = \frac{\text{Total number of specialist days per admission per patient}}{\text{Total number of days per admission per patient}}$$

7.2.2.2.9 Overall cancers

For all cancers combined, the DRR was higher among the youngest age group (aged 0-4 years at diagnosis); it was statistically different for all age groups, except cases aged 15-19. The rates ranged from 23% to 27% lower than cases aged 0-4. The rate of hospital stays increased significantly in relation to year of diagnosis (DRR=1.04: 95% CI:1.03-1.06), deprivation levels (DRR=1.02, 95%CI: 1.01-1.04) and amount of specialist care (DRR=1.26, 95%CI: 1.11-1.44). Relapsed cases had 2.39-times significantly higher DRR than non-relapsed cases. Cases initially treated with radiotherapy alone, surgery alone, a combination of chemotherapy and surgery, radiotherapy and surgery, a combination of all, or had no record of treatment had significantly shorter hospital stays

than cases treated with chemotherapy alone by 78%, 74%, 28%, 85%, 45% and 23%, respectively.

Table 57: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for all cancers combined (n=3,151)

Characteristics	DRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.13	1.02-1.25	0.230
Age at diagnosis			
0-4	1 (ref)		
5-9	0.77	0.64-0.94	0.010
10-14	0.73	0.60-0.88	0.001
15-19	1.04	0.87-1.23	0.691
20-24	0.75	0.64-0.89	0.001
25-29	0.77	0.65-0.90	0.002
Year of diagnosis	1.04	1.03-1.06	<0.001
Deprivation*	1.02	1.01-1.04	<0.001
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.92	0.76-1.10	0.350
Proportion of specialist care[¥]	1.26	1.11-1.44	0.001
Relapsed			
Yes	1 (ref)		
No	2.39	2.06-2.78	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.22	0.15-0.32	<0.001
Surgery alone	0.26	0.22-0.30	<0.001
Chemotherapy and radiotherapy	1.13	0.92-1.38	0.238
Chemotherapy and surgery	0.72	0.63-0.83	<0.001
Radiotherapy and surgery	0.15	0.11-0.19	<0.001
Chemotherapy, radiotherapy and surgery	0.55	0.42-0.74	<0.001
No recorded treatment	0.77	0.65-0.90	0.001

Abbreviations: DRR = number of days in hospital rate ratio; ref = reference category

[β]The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.3 Relapsed during study period

The rate of hospital admissions and hospital stays adjusting for person-years and days at risk, as well as patient characteristics was assessed to identify the effect of relapse on patterns of hospital activity, compared to those individuals who never relapsed.

Overall, there were no differences in the pattern of admissions or length of stay among patient characteristics for relapsed and non-relapsed cases (Table 58). The rate of admission decreased with increasing age at diagnosis, and increased for every yearly increase in year of diagnosis. DRR was higher among females compared with males.

Table 58: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for non-relapsed and non-relapsed cases (n=2,734 and 417 respectively)

Characteristics	**Non-relapsed cases**			**Relapsed cases**		
	HRR$^{\beta}$	**95% CI**	***P*-value**	**HRR$^{\beta}$**	**95% CI**	***P*-value**
Gender						
Male	1 (ref)			1 (ref)		
Female	1.04	0.96-1.13	0.346	1.10	0.91-1.32	0.314
Age at diagnosis	0.98	0.98-0.99	<0.001	0.97	0.96-0.98	<0.001
Year of diagnosis	1.08	1.07-1.10	<0.001	1.07	1.04-1.10	<0.001
Deprivation	1.02	0.80-1.09	0.01	1.01	0.98-1.04	0.555
Ethnicity						
Non-South Asian	1 (ref)			1 (ref)		
South Asian	0.93	0.80-1.09	0.362	0.77	0.54-1.10	0.157
Proportion of specialist care						
Mostly specialist admission	1 (ref)			1 (ref)		
Some specialist admission	0.71	0.62-0.81	<0.001	0.89	0.61-1.29	0.524
Limited specialist admission	0.78	0.70-0.87	<0.001	1.01	0.79-1.29	0.933
Initial treatment						
Chemotherapy alone	1 (ref)			1 (ref)		
Radiotherapy alone	0.18	0.13-0.25	<0.001	0.26	0.10-0.71	0.009
Surgery alone	0.17	0.15-0.19	<0.001	0.15	0.09-0.23	<0.001
Chemotherapy and radiotherapy	1.23	1.04-1.46	0.017	0.96	0.70-1.33	0.812
Chemotherapy and surgery	0.69	0.61-0.77	<0.001	0.73	0.58-0.92	0.008
Radiotherapy and surgery	0.14	0.11-0.17	<0.001	0.25	0.12-0.56	0.001
Chemotherapy, radiotherapy and surgery	0.62	0.46-0.81	<0.001	1.09	0.75-1.59	0.658
No recorded treatment	0.53	0.46-0.61	<0.001	0.48	0.35-0.68	<0.001

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

$^{\beta}$The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

Table 59: Inpatient number of days in hospital rate ratio (DRR) by demographic and clinical characteristics for non-relapsed and relapsed cases (n=2,734 and 417 respectively)

Characteristics	Non-relapsed			Relapsed		
	DRR$^{\beta}$	95% CI	*P*-value	DRR$^{\beta}$	95% CI	*P*-value
Gender						
Male	1 (ref)			1 (ref)		
Female	1.14	1.02-1.28	0.017	1.06	0.86-1.30	0.572
Age at diagnosis						
0-4	1 (ref)			1 (ref)		
5-9	0.76	0.61-0.95	0.015	0.85	0.59-1.24	0.398
10-14	0.66	0.53-0.82	<0.001	1.00	0.73-1.37	0.997
15-19	0.66	0.83-1.23	0.921	1.06	0.78-1.45	0.708
20-24	1.01	0.62-0.91	0.003	0.74	0.52-1.06	0.097
25-29	0.75	0.65-0.94	0.008	0.65	0.45-0.93	0.018
Year of diagnosis	1.05	1.03-1.06	<0.001	1.06	1.03-1.09	<0.001
Deprivation*	1.03	1.01-1.06	0.002	1.03	1.00-1.06	0.098
Ethnicity						
Non-South Asian	1 (ref)			1 (ref)		
South Asian	0.95	0.78-1.16	<0.001	0.71	0.48-1.04	0.075
Amount of specialist care¥	1.31	1.13-1.51	<0.001	0.95	0.69-1.29	0.727
Initial treatment						
Chemotherapy alone	1 (ref)			1 (ref)		
Radiotherapy alone	0.21	0.21-0.32	<0.001	0.11	0.10-0.76	0.013
Surgery alone	0.27	0.22-0.32	<0.001	0.94	0.07-0.17	<0.001
Chemotherapy and radiotherapy	1.19	0.94-1.50	0.14	0.94	0.66-1.34	0.749
Chemotherapy and surgery	0.74	0.63-0.87	<0.001	0.64	0.49-0.82	<0.001
Radiotherapy and surgery	0.13	0.10-0.17	<0.001	0.44	0.19-1.01	0.054
Chemotherapy, radiotherapy and surgery	0.48	0.34-0.68	<0.001	0.67	0.44-1.01	0.053
No recorded treatment	0.83	0.69-0.99	0.039	0.38	0.26-0.55	<0.001

Abbreviations: DRR = number of days in hospital rate ratio; ref = reference category

$^{\beta}$The number of days in hospital rate ratio was estimated adjusting for person-days at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.4 Not survived during study period

The rate of admissions was analysed separately among cases who survived for the entire duration of the study period compared with cases who died.

The difference was in the level of specialist care admissions, with those who remained alive having a 22% significantly lower rate of admissions when cases had limited specialist care admissions compared with cases receiving mostly specialist care admissions, while cases who died had 18% more admissions compared with those who received a higher proportion of specialist care admissions.

Table 60: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for survived and deceased cases (n=2,493 and N=658)

Characteristics	Survived			Deceased		
	HRR[β]	95% CI	*P*-value	HRR[β]	95% CI	*P*-value
Gender						
Male	1 (ref)			1 (ref)		
Female	1.19	1.12-1.28	<0.001	1.03	0.91-1.16	0.681
Age at diagnosis	0.97	0.97-0.98	<0.001	0.97	0.96-0.98	<0.001
Year of diagnosis	1.15	1.14-1.16	<0.001	1.06	1.04-1.07	<0.001
Deprivation	1.01	1.00-1.02	0.220	1.00	0.98-1.02	0.803
Ethnicity						
Non-South Asian	1 (ref)			1 (ref)		
South Asian	1.02	0.91-1.15	0.702	0.95	0.76-1.18	0.628
Proportion of specialist care						
Mostly specialist admission	1 (ref)			1 (ref)		
Some specialist admission	0.82	0.74-0.91	<0.001	0.95	0.76-1.18	0.632
Limited specialist admission	0.78	0.71-0.84	<0.001	1.18	1.02-1.37	0.023
Relapsed						
No	1 (ref)			1 (ref)		
Yes	1.66	1.47-1.88	<0.001	1.05	0.93-1.19	0.413
Initial treatment						
Chemotherapy alone	1 (ref)			1 (ref)		
Radiotherapy alone	0.23	0.18-0.30	<0.001	0.18	0.11-0.28	<0.001
Surgery alone	0.21	0.19-0.24	<0.001	0.31	0.23-0.42	<0.001
Chemotherapy and radiotherapy	1.08	0.94-1.25	0.265	0.82	0.68-0.98	0.033
Chemotherapy and surgery	0.59	0.54-0.64	<0.001	0.95	0.81-1.12	0.576
Radiotherapy and surgery	0.24	0.20-0.28	<0.001	0.19	0.12-0.30	<0.001
Chemotherapy, radiotherapy and surgery	0.87	0.71-1.06	0.169	0.63	0.49-0.82	<0.001
No recorded treatment	0.37	0.33-0.41	<0.001	0.76	0.62-0.92	0.004

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

[β]The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.5 Distribution of HRR by year of diagnosis prior- and post-introduction of payment by result

The rate of admissions adjusting for patient characteristics and years at risk was analysed before and after the introduction of the NHS payment by results policy in 2003/2004 (details of this policy can be found in Section 4.6.2). The rate of admission was 53% higher after introducing the payment by result policy, compared with the rate of admission among cases diagnosed before introducing that policy, and it was statistically significant.

Table 61: Inpatient hospital admission rate ratio (HRR) by demographic and clinical characteristics for overall cancers (n=3,151)

Characteristics	HRR$^{\beta}$	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.05	0.97-1.14	0.230
Age at diagnosis	0.98	0.98-0.99	<0.001
Year of diagnosis			
Before introducing payment by results	1 (ref)		
After introducing payment by results	1.53	1.41-1.66	<0.001
Deprivation	1.01	1.00-1.03	0.026
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.93	0.80-1.07	0.302
Proportion of specialist care			
Mostly specialist admission	1 (ref)		
Some specialist admission	0.69	0.61-0.78	<0.001
Limited specialist admission	0.74	0.67-0.82	<0.001
Relapsed			
No	1 (ref)		
Yes	2.51	2.24-2.80	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.18	0.13-0.24	<0.001
Surgery alone	0.16	0.14-0.19	<0.001
Chemotherapy and radiotherapy	1.20	1.03-1.40	0.022
Chemotherapy and surgery	0.68	0.61-0.76	<0.001
Radiotherapy and surgery	0.14	0.11-0.17	<0.001
Chemotherapy, radiotherapy and surgery	0.77	0.62-0.96	0.020
No recorded treatment	0.52	0.46-0.59	<0.001

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

$^{\beta}$The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.6 Distribution of hospital admission rate ratio after completion of cancer treatment among cases treated with a BMT compared with cases not treated with a BMT

During the post-treatment period, females had lower rates of admissions than males (HRR= 20%, 95%CI: 6-33%,*P*-value = 0.008). The number of admissions per person-year increased with increasing age at diagnosis by year, and with increasing year of diagnosis, i.e. TYA survivors had more admissions after treatment completion compared with childhood survivors. The increase in admissions by age was consistent for the main diagnostic groups and increased ranging from 3% to 17% after treatment completion, except for germ cell tumour survivors, where the rate of admission decreased by 5% with single year increases in age (data not shown). Cases diagnosed earlier had significantly fewer admissions compared with cases diagnosed more recently (Table 62). Cases with a BMT had almost double the rate of admissions than cases with no BMT, and was seven-times greater among cases with relapses compared with non-relapsed cases, in which both were significant differences. The rate of admission and relapse was between 6- and 47-times by diagnostic group. Cases treated with radiotherapy alone, surgery alone, and a combination of radiotherapy and surgery had lower rates of admission compared with cases treated with chemotherapy alone.

Table 62: Inpatient hospital admission rate ratio (HRR) after completion of cancer treatment n=1,723 (cases with admissions after treatment completion)

Characteristics	HRR[β]	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	0.79	0.67-0.94	0.008
Age at diagnosis	1.04	1.03-1.05	<0.001
Year of diagnosis	1.16	1.13-1.19	<0.001
Deprivation	1.01	0.99-1.04	<0.001
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.81	0.58-1.13	0.314
Proportion of specialist care			
Mostly specialist admission	1 (ref)		
Some specialist admission	1.12	0.85-1.48	0.419
Limited specialist admission	0.84	0.69-1.04	0.110
BMT			
No	1 (ref)		
Yes	1.93	1.28-2.93	0.002
Relapsed			
No	1 (ref)		
Yes	7.06	4.95-10.06	<0.001
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	0.25	0.15-0.42	<0.001
Surgery alone	0.29	0.23-0.36	<0.001
Chemotherapy and radiotherapy	0.57	0.40-0.82	0.003
Chemotherapy and surgery	0.64	0.50-0.82	0.001
Radiotherapy and surgery	0.18	0.13-0.26	<0.001
Chemotherapy, radiotherapy and surgery	1.23	0.75-0.02	0.418
No recorded treatment	0.39	0.18-0.84	0.016

Abbreviations: HRR = hospital admission rate ratio; ref = reference category

[β]The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

¥ $\text{Amount of specialist care} = \frac{\text{Total number of specialist admission per patient}}{\text{Total number of admission per patient}}$

7.2.6.1 Distribution of HRR after completion of cancer treatment among cases treated with a BMT: leukaemia cases compared with other diagnostic groups

A subset analysis for cases treated with a BMT compared the pattern of admissions after completion of cancer treatment among leukaemia survivors with all other cancer survivors who received a BMT (Table 63). It was found that leukaemia cases treated with a BMT had higher rates of admission compared with cases with any other cancer type, but this was not significant (HRR= 1.05, 95%CI:0.42-2.62). Additionally, relapsed cases had three-times higher numbers of admissions per person-year than cases with no relapse.

Table 63: Inpatient hospital admission rate ratio (HRR) for cases treated with a BMT after completion of cancer treatment n=68

Characteristics	HRR$^{\beta}$	95% CI	*P*-value
Gender			
Male	1 (ref)		
Female	1.27	0.50-3.27	0.615
Age at diagnosis	1.05	0.97-1.13	0.199
Year of diagnosis	1.13	0.91-1.16	0.069
Deprivation	1.03	0.14-1.39	0.643
Ethnicity			
Non-South Asian	1 (ref)		
South Asian	0.44	0.19-1.90	0.389
Proportion of specialist care			
Mostly specialist admission	1 (ref)		
Some specialist admission	0.57	0.15-2.22	0.420
Limited specialist admission	1.44	0.27-7.77	0.668
Cancer type			
Other diagnostic group	1 (ref)		
Leukaemia	1.15	0.42-2.85	0.762
Relapsed			
No	1 (ref)		
Yes	3.95	1.62-9.66	0.003
Initial treatment			
Chemotherapy alone	1 (ref)		
Radiotherapy alone	NA		NA
Surgery alone	NA		NA
Chemotherapy and radiotherapy	0.17	0.03-0.99	0.049
Chemotherapy and surgery	2.57	0.82-8.01	0.104
Radiotherapy and surgery	NA		NA
Chemotherapy, radiotherapy and surgery	2.57	0.03-1.32	0.094
No recorded treatment	NA	NA	

Abbreviations: HRR = hospital admission rate ratio; NA = not applicable i.e. there were no individuals in this category; ref = reference category

$^{\beta}$The hospital admission rate ratio was estimated adjusting for person-years at risk

*Deprivation criteria was classified using Townsend score

7.2.7 Sensitivity analysis before and after identifying type of initial treatment

The following section conducts an in-depth sensitivity analysis to identify the differences that can be detected, which could affect the outcome if the initial treatment was not identified. This took the form of comparing the results from two chapters: Chapter 6 and 7.

7.2.7.1 Impact on the descriptive chapter results

The current thesis is interested in identifying the initial type of treatment for primary diagnosis, which was the planned treatment after being diagnosed with cancer. However, the study data sources, the cancer register and HES, do not identify the initial treatment (the first-line treatment). For example, if cases received chemotherapy, radiotherapy and surgery they were assigned as having them all, regardless of the time gap between the date of diagnosis and the treatment, or the time difference between complex modalities.

The sensitivity analysis was done to compare the distributions of cases by type of treatment received after diagnosis, using what was recorded in the cancer register and HES (all recorded treatments) with the initial treatment only that was identified using a predefined proxy; and that was the study main outcome.

After the sensitivity analysis (identifying the initial treatments), the distribution in the type of treatment modality was altered for all diagnostic groups especially lymphoma. The major difference was among chemotherapy alone and surgery, where the percentage of cases allocated to them increased, while a combination of chemotherapy and radiotherapy decreased, as did all modalities in combination (Table 64 and Table 65).

Table 64: Distribution of cases by type of treatment (all treatment) and diagnostic group

Diagnostic group ICCC-3	Leukaemia		Lymphoma		CNS		Neuroblastoma		Renal tumours		Bone tumours		STS		Germ cell tumours		Overall cancers	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Chemotherapy alone	505	82	365	57	45	10	26	27	28	30	49	33	52	21	35	6	1,105	39
Radiotherapy alone	<5	0	21	3	29	6	<5	0	<5	0	<5	1	4	2	<5	0	60	2
Surgery alone*	<5	0	#	2	114	25	18	19	19	21	11	7	62	25	127	23	362	13
Chemotherapy and radiotherapy	60	10	106	17	40	9	5	5	<5	3	12	8	37	15	<5	1	267	9
Chemotherapy and surgery	14	2	72	11	43	9	25	26	37	40	53	35	38	15	279	49	561	20
Radiotherapy and surgery	<5	0	9	1	34	7	<5	1	<5	0	<5	3	6	2	91	16	145	5
Chemotherapy, radiotherapy and surgery	<5	0	21	3	55	12	5	5	<5	4	5	3	14	6	12	2	118	4
No recorded treatment	30	5	31	5	103	22	16	17	<5	1	14	9	39	15	15	3	249	9
Total¥	615	100	635	100	463	100	96	100	92	100	150	100	252	100	564	100	2,867	100

* Only cancer related major surgeries, detail of surgery code is included in the appendices

¥ includes cases with minor surgeries, cases died before treatment started, no record of treatment

figures removed to avoid disclosure of potentially identifiable data

Table 65: Distribution of cases by type of treatment (initial treatment) and diagnostic group

Diagnostic group ICCC-3	Leukaemia		Lymphoma		CNS		Neuroblastoma		Renal tumours		Bone tumours		STS		Germ cell tumours		Overall cancers	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Chemotherapy alone	528	86	399	63	47	10	26	27	29	32	56	37	55	22	40	7	1,180	41
Radiotherapy alone	<5	0	24	4	27	6	0	0	0	0	<5	1	<5	2	<5	0	62	2
Surgery alone*	<5	0	#	2	133	29	24	25	22	24	19	13	76	30	130	23	417	15
Chemotherapy and radiotherapy	47	8	78	12	34	7	5	5	<5	2	8	5	36	14	#	1	215	7
Chemotherapy and surgery	14	2	75	12	45	10	27	28	35	38	52	35	42	17	278	49	568	20
Radiotherapy and surgery	<5	0	11	2	31	7	<5	1	0	0	<5	1	#	2	89	16	139	5
Chemotherapy, radiotherapy and surgery	<5	0	16	3	48	10	<5	4	<5	4	<5	3	11	4	8	1	97	3
No recorded treatment	20	3	20	3	98	21	9	9	0	0	#	5	23	9	12	2	189	7
Total¥	615	100	635	100	463	100	96	100	92	100	150	100	252	100	564	100	2,867	100

* Only cancer related major surgeries, detail of surgery code is included in the appendices

¥ includes cases with minor surgeries, cases died before treatment started, no record of treatment

figures removed to avoid disclosure of potentially identifiable data

7.2.7.2 Impact on the modelling process

A subset analysis was done to model the data using all treatments and another model with initial treatment and the pattern of admission showed similar results by patient characteristics (data not shown).

7.3 Summary

Negative binomial modelling provided a better model fit in describing the variation in hospital activity. The factors that influenced the rate of admissions and hospital durations varied by cancer subtype. For all cancers combined, there were no statistical differences between gender and rate of admission. However, there were significant differences in hospital stays and gender among cases diagnosed with leukaemia and CNS tumours. Female cases with leukaemia had significantly longer hospital stays than males, while females with CNS tumours had significantly shorter stays than males.

Rates of admissions were significantly higher among younger age groups for the majority of diagnostic groups, except for renal tumours. The relationship between age at diagnosis and length of stay was significant among those with leukaemia, STS and germ cell tumours. For leukaemia and STS, a longer length of stay was associated with increased age at diagnosis, while for germ cell tumours a shorter length of stay was associated with increased age at diagnosis. The rate of admission increased by year of diagnosis among most diagnostic groups. Additionally, there were significant increases in the rate of hospital days by year of diagnosis, i.e. cases stayed longer in hospital when cases were diagnosed more recently, compared with cases diagnosed earlier on.

The relationship between deprivation and rate of admission was significant among cases diagnosed with CNS tumours, and it was higher in most deprived areas. Similarly, most deprived cases had the longest hospital stays compared with the least deprived cases, when diagnosed with CNS and germ cell tumours. Differences by ethnic group were only significant among cases diagnosed with STS, where South Asians had lower rates of admission and shorter hospital stays than non-South Asians.

The rate of admission was significantly higher among cases who received a higher proportion of admissions in specialist units, when diagnosed with renal tumours or germ cell tumours. The proportion of specialist care was significantly related to length of stay among survivors of lymphoma, CNS, STS, renal tumours and germ cell tumours. Lymphoma, renal tumours and STS had longer stays when they received a higher proportion of care in specialist units, whilst CNS tumours and germ cell tumours had shorter stays when they received a higher proportion of care in specialist units.

Relapsed cases had significantly higher rates of admissions and longer hospital stays than non-relapsed cases and this difference was statistically significant.

Cases treated with chemotherapy alone had the highest rate of admissions and longest hospital stays, while cases who received radiotherapy had the lowest rate of admission and shortest hospital stays for most diagnostic groups. Cases treated with a BMT had significantly higher rates of admission after completion of cancer treatment compared to those who did not receive a BMT.

Chapter 8 Morbidity Related to Hospitalisation

8.1 Introduction

This chapter includes a description of the cause-specific hospitalisations among the cancer cohort, followed by a summary of the difference in admission patterns before and after cancer treatment, according to the cause of hospital admission and cancer type (Aim 4).

In addition, the median time to first admission for all causes combined and by specific cause are explored. This was done to provide healthcare providers and patients with an overview of the healthcare burden following cancer.

Finally, excess hospitalisation rates were estimated by comparing hospital admissions after completion of cancer treatment among cancer cohorts with hospital admissions among age, sex and year of admission in the matched background population (Questions 4 and 5).

8.2 Overview of type of morbidity for the complete follow-up period

8.2.1 Distribution of inpatient admissions by primary cause of admission (ICD-10) and diagnostic group (ICCC-3)

During the post-diagnosis period for all diagnostic groups, the majority of inpatient admissions were attributable to neoplasms, followed by admissions classified as factors influencing health status and contact with health services. Individuals aged 0-29 diagnosed with leukaemia had a higher number of inpatient admissions compared with other diagnostic groups, followed by lymphoma having 37% and 20% respectively from date of diagnosis onward (Table 66 and Table 67).

Table 66: The distribution of inpatient admissions (spells) by main cause of inpatient admissions (ICD-10) and diagnostic group (ICCC-3)

Admission type ICD-10	Leukaemia		Lymphoma		CNS		Neuroblastoma		Retinoblastomas		Renal tumours	
	N	%	N	%	N	%	N	%	N	%	N	%
Certain infectious and parasitic diseases	538	2	110	1	65	1	46	2	7	1	44	3
Neoplasms	19,010	78	10,759	80	4,372	63	1,860	77	633	75	1,079	65
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	907	4	362	3	171	2	90	4	19	2	48	3
Endocrine, nutritional and metabolic diseases	79	0	39	0	74	1	8	0	1	0	23	1
Mental and behavioural disorders	7	0	15	0	6	0	1	0	0	0	0	0
Diseases of the nervous system	33	0	19	0	213	3	27	1	0	0	1	0
Diseases of the eye and adnexa	50	0	12	0	89	1	1	0	9	1	1	0
Diseases of the ear and mastoid process	92	0	8	0	23	0	6	0	5	1	8	0
Diseases of the circulatory system	55	0	44	0	12	0	7	0	0	0	20	1
Diseases of the respiratory system	482	2	197	1	134	2	34	1	9	1	59	4
Diseases of the digestive system	332	1	241	2	143	2	56	2	2	0	44	3
Diseases of the skin and subcutaneous tissue	87	0	64	0	31	0	6	0	3	0	11	1
Diseases of the musculoskeletal system and connective tissue	148	1	101	1	57	1	10	0	1	0	6	0

Admission type ICD-10	Leukaemia		Lymphoma		CNS		Neuroblastoma		Retinoblastomas		Renal tumours	
	N	%	N	%	N	%	N	%	N	%	N	%
Diseases of the genitourinary system	68	0	76	1	32	0	6	0	1	0	39	2
Pregnancy, childbirth and the puerperium	67	0	282	2	123	2	1	0	0	0	10	1
Certain conditions originating in the perinatal period	1	0	0	0	1	0	0	0	0	0	0	0
Congenital malformations, deformations and chromosomal abnormalities	18	0	15	0	83	1	6	0	1	0	23	1
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	722	3	528	4	559	8	115	5	38	5	132	8
Injury, poisoning and certain other consequences of external causes	661	3	195	1	168	2	58	2	21	3	50	3
External causes of morbidity and mortality	0	0	0	0	0	0	0	0	0	0	0	0
Factors influencing health status and contact with health services	1,145	5	374	3	614	9	82	3	90	11	68	4
Codes for special purposes	0	0	0	0	0	0	0	0	0	0	0	0
All admissions	24,502	100	13,441	100	6,970	100	2,420	100	840	100	1,666	100

Abbreviations: N = number of admissions; CNS = central nervous system

Table 67: The distribution of inpatient admissions (1997-2011) by main cause of admissions (ICD-10) and diagnostic group (ICCC-3) (continued)

Admission type (ICD-10)	Hepatic tumours		Bone tumours		STS		Germ cell tumours		Other epithelial neoplasms		Other unspecified neoplasm		Overall cases	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Certain infectious and parasitic diseases	12	2	32	1	64	1	51	1	9	0	2	2	980	1
Neoplasms	379	72	3,254	79	3,592	75	2,770	68	1,355	55	69	62	49,132	75
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	5	1	135	3	172	4	78	2	23	1	4	4	2,014	3
Endocrine, nutritional and metabolic diseases	2	0	13	0	33	1	41	1	44	2	1	1	358	1
Mental and behavioural disorders	0	0	1	0	4	0	12	0	1	0	0	0	47	0
Diseases of the nervous system	0	0	6	0	18	0	25	1	13	1	0	0	355	1
Diseases of the eye and adnexa	1	0	3	0	16	0	14	0	7	0	0	0	203	0
Diseases of the ear and mastoid process	3	1	3	0	20	0	7	0	7	0	0	0	182	0
Diseases of the circulatory system	5	1	19	0	24	1	37	1	20	1	2	2	245	0
Diseases of the respiratory system	23	4	28	1	69	1	54	1	28	1	3	3	1,120	2
Diseases of the digestive system	8	2	51	1	82	2	131	3	169	7	3	3	1,262	2
Diseases of the skin and subcutaneous tissue	0	0	30	1	35	1	38	1	28	1	1	1	334	1

Admission type (ICD-10)	Hepatic tumours		Bone tumours		STS		Germ cell tumours		Other epithelial neoplasms		Other unspecified neoplasm		Overall cases	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Diseases of the musculoskeletal system and connective tissue	3	1	59	1	48	1	48	1	51	2	0	0	532	1
Diseases of the genitourinary system	1	0	39	1	44	1	98	2	55	2	0	0	459	1
Pregnancy, childbirth and the puerperium	5	1	31	1	60	1	59	1	171	7	1	1	810	1
Certain conditions originating in the perinatal period	0	0	0	0	1	0	2	0	0	0	0	0	5	0
Congenital malformations, deformations and chromosomal abnormalities	0	0	2	0	24	1	21	1	7	0	0	0	200	0
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	21	4	89	2	178	4	274	7	213	9	8	7	2,877	4
Injury, poisoning and certain other consequences of external causes	17	3	135	3	126	3	153	4	54	2	3	3	1,641	2
External causes of morbidity and mortality	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Factors influencing health status and contact with health services	39	7	174	4	176	4	169	4	223	9	15	13	3,169	5
Codes for special purposes	0	0	0	0	0	0	0	0	0	0	0	0	0	0
All causes	524	100	4,104	100	4,786	100	4,082	100	2,478	100	112	100	65,925	100

Abbreviations: N = number of admissions; STS = soft tissue sarcoma

8.2.1.1 Distribution of inpatient admissions by primary cause of admission (ICD-10) and period of admission

Admissions for neoplasms were common among the cancer cohort in both on treatment and post-treatment periods (Table 68). Admission for ‘certain infectious diseases’, ‘neoplasms’, ‘diseases of the blood’, ‘diseases of the respiratory’, ‘certain conditions originating in the perinatal period system’ and ‘symptoms, signs and abnormal clinical and laboratory findings’ were more common during the on treatment phase (Figure 57, Figure 58 and Figure 59). The remaining causes included ‘endocrine diseases’ (including metabolic disorders 40%, disorders of other endocrine glands 35%, diabetes mellitus 8%, disorders of the thyroid gland 8% – data not shown), ‘mental disorders’ (the 47 mental inpatient admissions – in total one third – were due to mental and behavioural disorders due to psychoactive substance use, while four out of seven mental inpatient admissions among leukaemia cases were for mood disorder – data not shown) and ‘musculoskeletal diseases’, which were more common during the post-treatment inpatient admissions compared to the on treatment phase.

Table 68: Number of inpatient admissions by period of admission and cause of admission (ICD-10)

	On treatment*		Post-treatment*		Total admission	
Admission type ICD-10	**N**	**%**	**N**	**%**	**N**	**%**
Certain infectious and parasitic diseases	764	1.56	175	1.44	939	1.54
Neoplasms	40,648	83.03	5,752	47.38	46,400	75.94
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1,617	3.30	338	2.78	1,955	3.20
Endocrine, nutritional and metabolic diseases	93	0.19	207	1.71	300	0.49
Mental and behavioural disorders	10	0.02	33	0.27	43	0.07
Diseases of the nervous system	134	0.27	142	1.17	276	0.45
Diseases of the eye and adnexa	59	0.12	98	0.81	157	0.26
Diseases of the ear and mastoid process	68	0.14	92	0.76	160	0.26
Diseases of the circulatory system	93	0.19	119	0.98	212	0.35
Diseases of the respiratory system	582	1.19	448	3.69	1,030	1.69
Diseases of the digestive system	490	1.00	535	4.41	1,025	1.68
Diseases of the skin and subcutaneous tissue	142	0.29	147	1.21	289	0.47
Diseases of the musculoskeletal system and connective tissue	179	0.37	286	2.36	465	0.76
Diseases of the genitourinary system	170	0.35	215	1.77	385	0.63
Pregnancy, childbirth and the puerperium	76	0.16	508	4.18	584	0.96
Certain conditions originating in the perinatal period	3	0.01	1	0.01	4	0.01
Congenital malformations, deformations and chromosomal abnormalities	58	0.12	109	0.90	167	0.27
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	1,499	3.06	1,003	8.26	2,502	4.10
Injury, poisoning and certain other consequences of external causes	847	1.73	654	5.39	1,501	2.46
Factors influencing health status and contact with health services	1,426	2.91	1,278	10.53	2,704	4.43
Total*	48,958	100	12,140	100	61,098	100

* Includes main diagnostic group where their initial treatment was identified using the study matrices, number of included cases was 2,867.

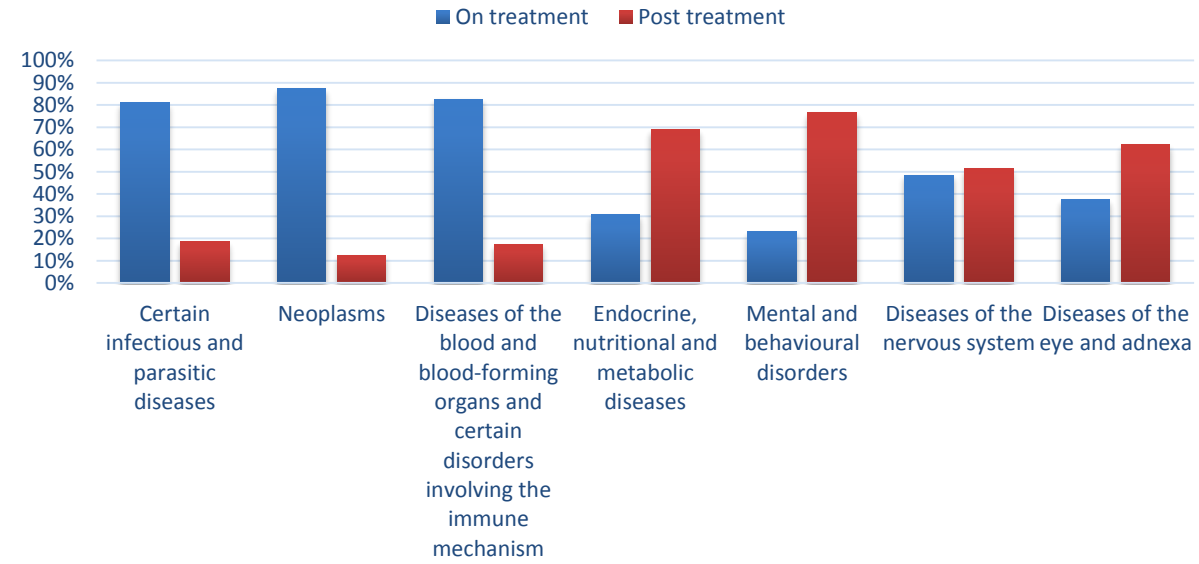


Figure 57: Percentage of inpatient admissions (1997-2011) for all cases aged 0-29 years at diagnosis by admission cause (ICD-10) according to period of admission (on and post-treatment)

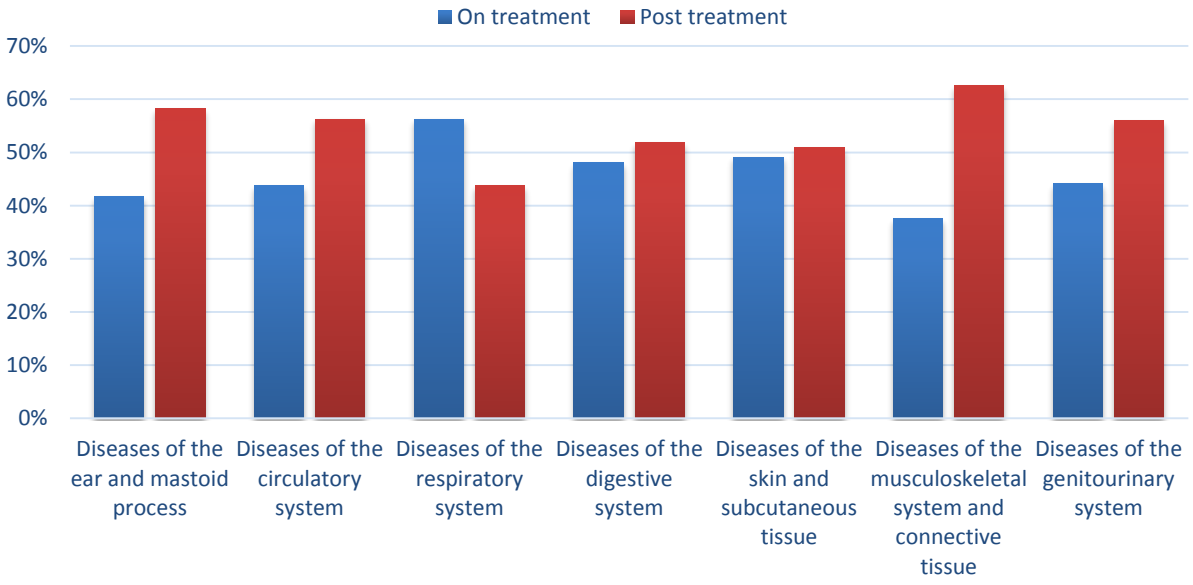


Figure 58: Percentage of inpatient admissions (1997-2011) for all cases aged 0-29 years at diagnosis by admission cause (ICD-10) according to period of admission (on and post-treatment)

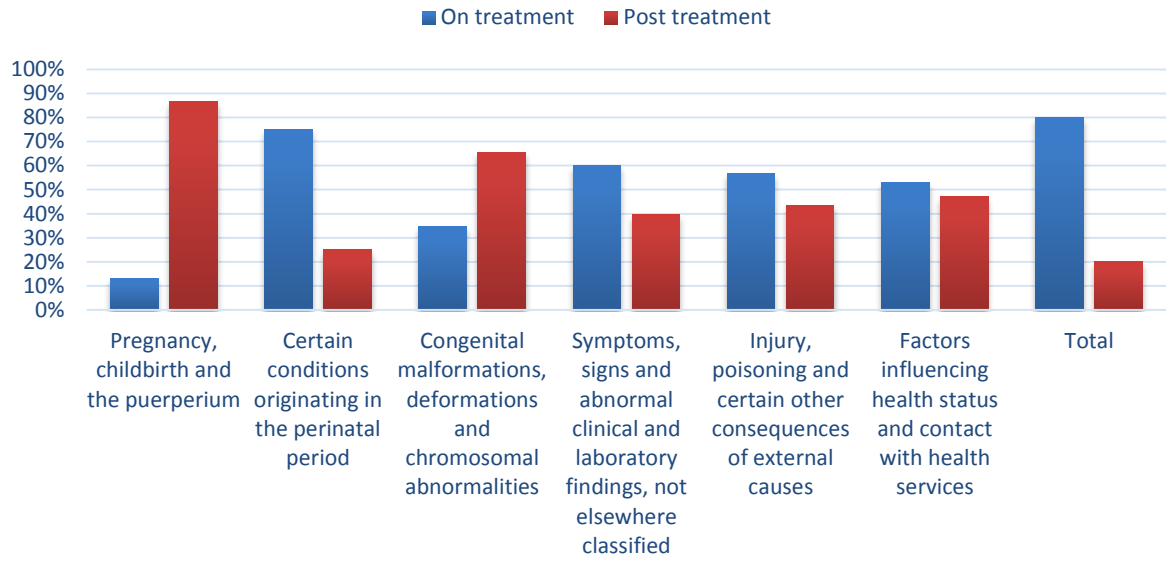


Figure 59: Percentage of inpatient admissions (1997-2011) for all cases aged 0-29 years at diagnosis by admission cause (ICD-10) according to period of admission (on and post-treatment)

8.2.1.2 Distribution of inpatient admissions by primary cause of admission (ICD-10), diagnostic group (ICCC-3) and period of admission (on treatment and post-treatment)

The rate of inpatient admissions during the study period (on treatment vs. post-treatment) was analysed by causes of specific admissions (ICD-10) and diagnostic group (ICCC-3) to assess the different rates of admission on and post-treatment.

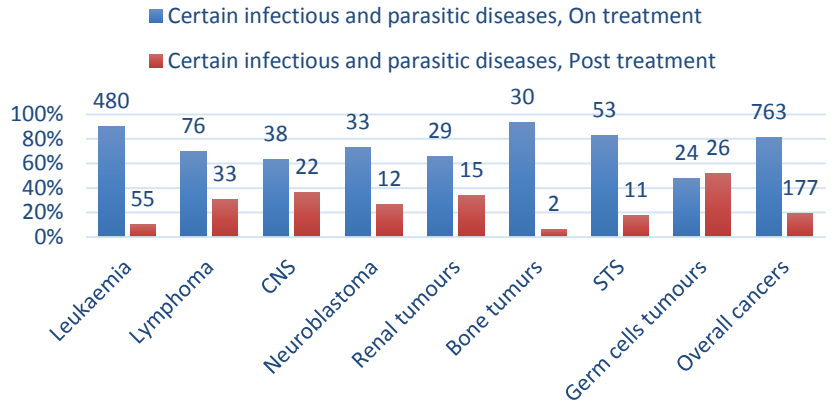
Admissions for ‘certain infectious diseases’ was higher during the on treatment phase, especially among cases diagnosed with bone tumours, with more than 90% of the total admissions occurring during the on treatment phase, compared with less than 10% during the post-treatment admissions (Figure 60).In contrast, cases diagnosed with germ cell tumours had a higher number of admissions for ‘certain infectious diseases’ during the post-treatment period.

Admissions for ‘endocrine, nutritional and metabolic diseases’ were higher during the post-treatment period, except for cases diagnosed with neuroblastoma or bone tumours, where admissions were higher during the on treatment phase (Figure 60).

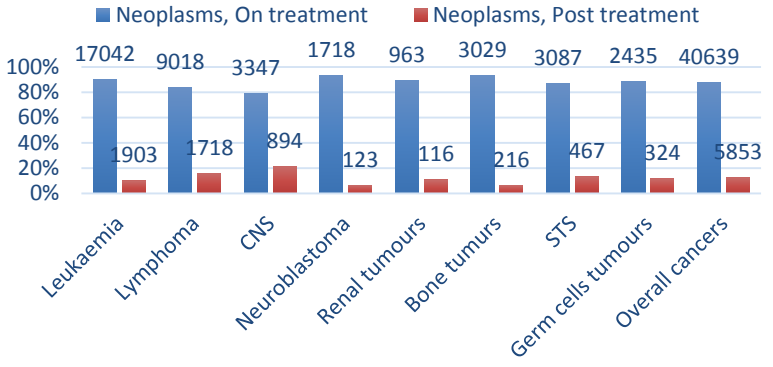
The admissions for ‘mental and behavioural disorders’, ‘diseases of the nervous system’ and ‘diseases of the eye’ were higher post-treatment compared to the on treatment phase for the majority of diagnostic groups, except for leukaemia, where the pattern of admission was in the opposite direction (higher during treatment than post-treatment) (Figure 61).

Similarly, bone tumour cases had different patterns of admission by period of admission from other diagnostic groups; they had a higher percentage of admissions during the on treatment phase than post-treatment phase for the following causes: ‘endocrine, nutritional and metabolic diseases’, ‘diseases of the nervous system’, ‘diseases of the eye’, ‘diseases of the ear’, ‘diseases of the digestive system’ and ‘diseases of the musculoskeletal system’ (Figure 60, Figure 61 and Figure 63). Cases admitted for ‘diseases of the circulatory system’ were higher during the post-treatment period, except for cases diagnosed with CNS and neuroblastoma (Figure 62).

Cases diagnosed with lymphoma, CNS, renal tumours and germ cell tumours had a higher number of admissions during the post-treatment phase than the on treatment phase, in contrast with other diagnostic groups for the admissions for ‘diseases of the respiratory system’ (Figure 62).



(a)



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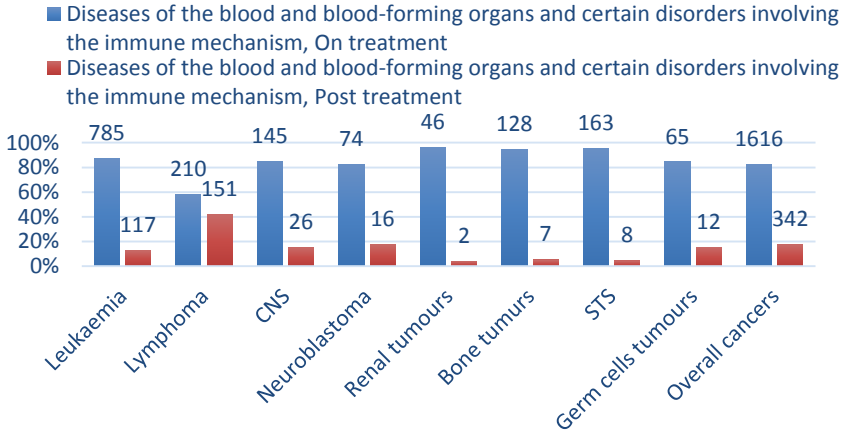

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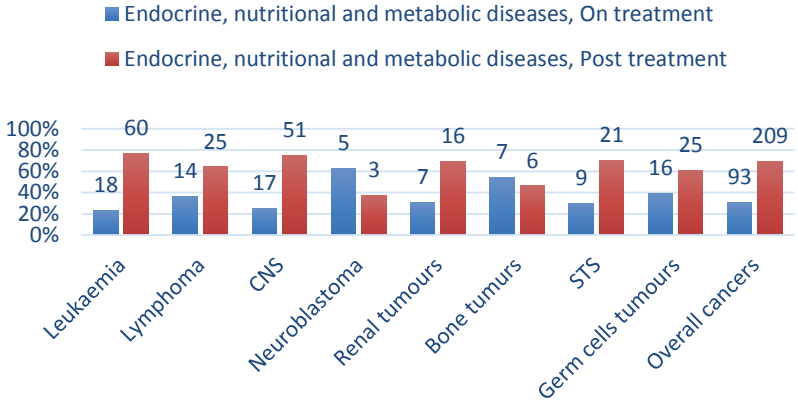


(d)

Figure 60:The percentage and number of admissions for ’certain infectious and parasitic diseases’ (a),’ neoplasms’ (b), ’diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism ’(c) and ‘endocrine, nutritional and metabolic diseases’ (d) and number of cases by diagnostic group and period of admission (on treatment and post-treatment)

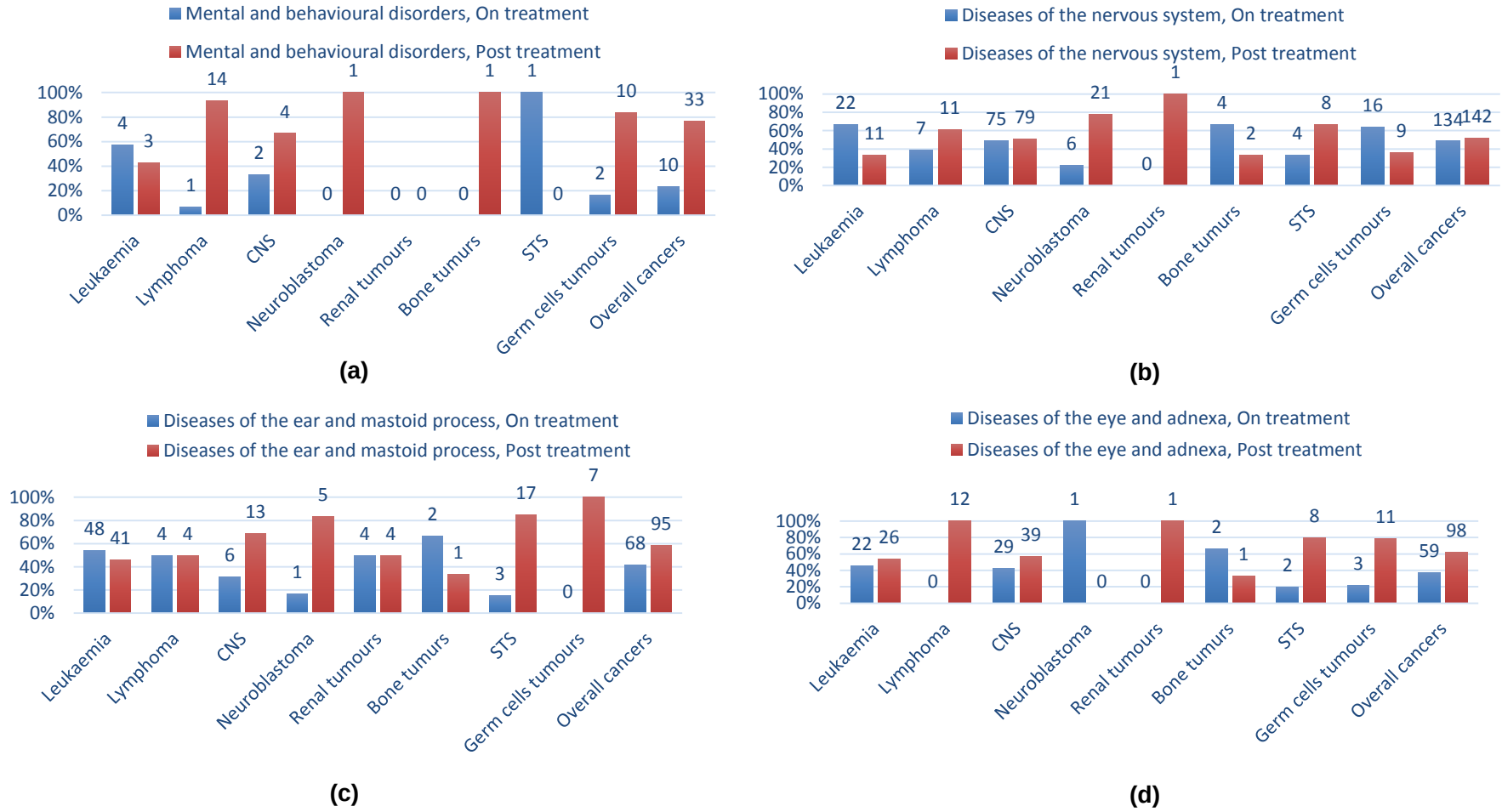


Figure 61:The percentage and number of admissions for ‘mental and behavioural disorders’ (a),‘diseases of the nervous system’ (b), diseases of ‘diseases of the eye and adnexa’ (c) and ‘disease of ear and mastoid process‘ (d) and number of cases by diagnostic group and period of admission (on treatment and post treatment)

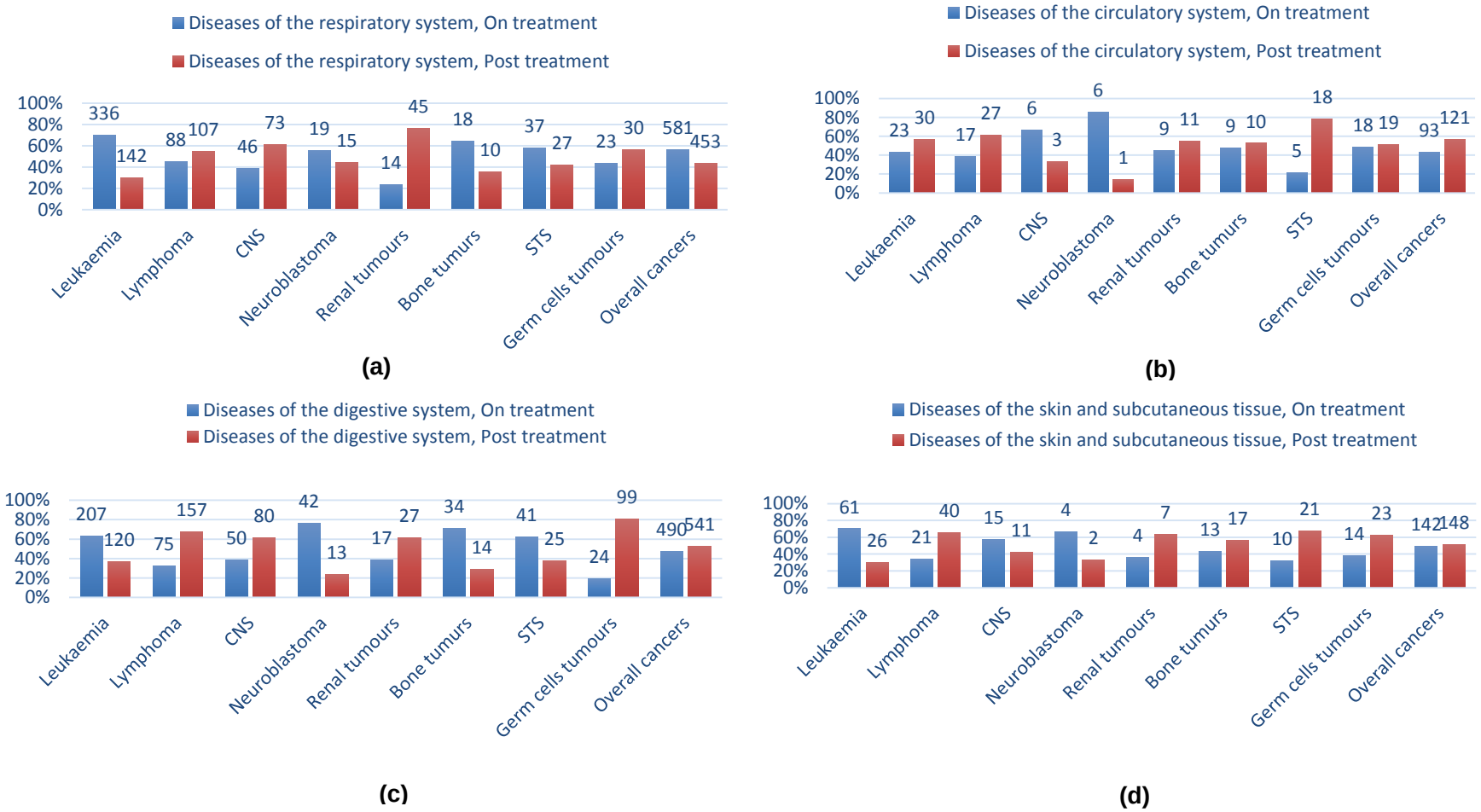
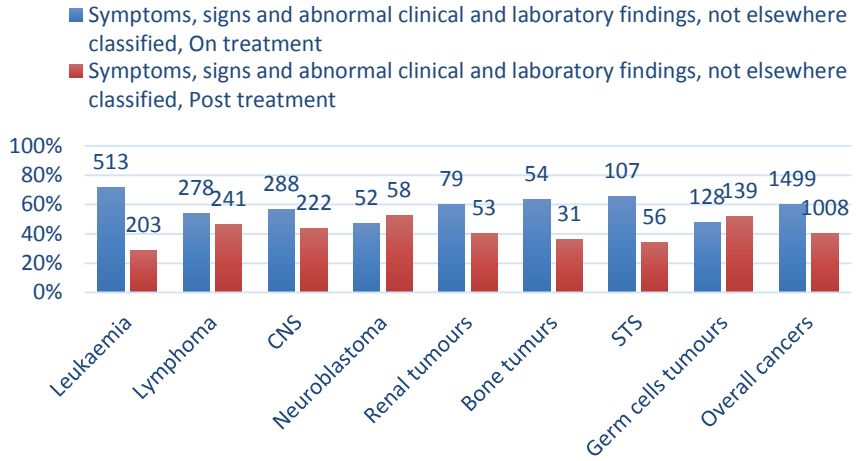
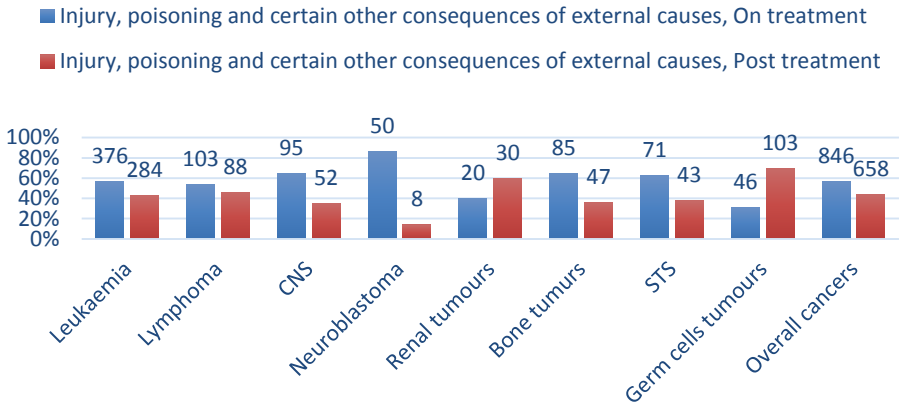


Figure 62:The percentage and number of admissions for ‘diseases of the respiratory system’ (a), ‘diseases of the circulatory system’ (b) number of cases, diseases of the digestive system’ (c) and ‘diseases of the skin and subcutaneous tissue’ (d) by diagnostic group and period of admission (on treatment and post-treatment)

Figure 63: The percentage and number of admissions ‘diseases of the musculoskeletal system and connective tissue’ (a), diseases of the genitourinary system (b), ‘pregnancy, childbirth and the puerperium’ (c) and ‘congenital malformations, deformations and chromosomal abnormalities’ (d) number of cases by diagnostic group and period of admission (on treatment and post-treatment)



(a)



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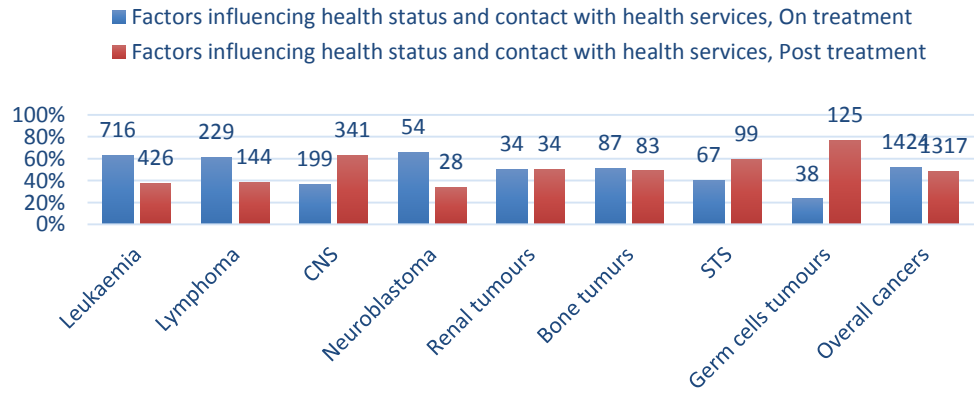

(c)

Figure 64: The percentage and number of admissions for 'symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified' (a), 'injury, poisoning and certain other consequences of external causes' (b) and 'factors influencing health status and contact with health services' (c) and number of cases by diagnostic group and period of admission (on treatment and post-treatment

8.2.2 Distribution of inpatient admissions by secondary causes of admission (ICD-10) and diagnostic group (ICCC-3)

In HES, the reason for admission, or the cause of admission was recorded in two groups. Primary diagnosis, i.e. the first diagnosis code of admission and defined as the main cause of admission, or the reason that caused the patient to receive hospital care. The other group was the secondary diagnosis of admission and is defined as any morbidity related to the primary diagnosis and external cause. For example, a patient could be admitted to hospital for heart disease and he might happen to have diabetes, the main cause will be to treat the heart disease and the secondary diagnosis is diabetes, as it is related to the primary cause of admission [203].

The majority of second causes of admissions were classified as ‘factors influencing health status’, followed by ‘neoplasms’ and ‘symptoms, signs and abnormal clinical and laboratory findings’ (Table 69 and Table 70). The rate for ‘musculoskeletal disease’ admissions were considerably high and represented the fourth highest secondary cause of admission, especially among neuroblastoma cases, having 23% of the total secondary admissions (n= 1,023 out of 4,400 neuroblastoma admissions).

Table 69: The distribution of secondary causes of admissions (ICD-10) by diagnostic group ICCC-3

Secondary cause of admission (ICD-10)	Leukaemia		Lymphoma		CNS		Neuroblastoma		Retinoblastoma		Renal tumours	
	N	%	N	%	N	%	N	%	N	%	N	%
Certain infectious and parasitic diseases	1,338	4	438	3	191	2	122	3	36	5	82	3
Neoplasms	3,203	10	1,429	9	1,308	12	942	21	67	10	551	18
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	2,138	7	686	4	318	3	267	6	45	6	136	4
Endocrine, nutritional and metabolic diseases	599	2	244	2	398	4	122	3	8	1	42	1
Mental and behavioural disorders	102	0	132	1	111	1	51	1	1	0	3	0
Diseases of the nervous system	313	1	193	1	1,014	9	115	3	0	0	12	0
Diseases of the eye and adnexa	148	0	47	0	282	3	39	1	16	2	12	0
Diseases of the ear and mastoid process	164	1	38	0	132	1	53	1	4	1	10	0
Diseases of the circulatory system	347	1	237	2	164	2	72	2	2	0	183	6
Diseases of the respiratory system	799	3	692	4	176	2	63	1	26	4	86	3
Diseases of the digestive system	706	2	382	2	238	2	72	2	4	1	85	3
Diseases of the skin and subcutaneous tissue	236	1	118	1	45	0	21	0	13	2	11	0
Diseases of the musculoskeletal system and connective tissue	403	1	1,519	10	567	5	1,023	23	116	17	461	15
Diseases of the genitourinary system	255	1	231	1	74	1	70	2	3	0	118	4
Pregnancy, childbirth and the puerperium	22	0	95	1	58	1	2	0	0	0	1	0
Certain conditions originating in the perinatal period	16	0	2	0	10	0	6	0	0	0	0	0
Congenital malformations, deformations and chromosomal abnormalities	322	1	50	0	317	3	61	1	20	3	92	3
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	8,200	26	1,143	7	1,224	11	212	5	25	4	189	6

Secondary cause of admission (ICD-10)	Leukaemia		Lymphoma		CNS		Neuroblastoma		Retinoblastoma		Renal tumours	
	N	%	N	%	N	%	N	%	N	%	N	%
Injury, poisoning and certain other consequences of external causes	526	2	219	1	141	1	55	1	15	2	43	1
External causes of morbidity and mortality	1,166	4	390	3	317	3	85	2	25	4	87	3
Factors influencing health status and contact with health services	10,086	32	7,313	47	3,703	34	947	22	274	39	933	30
Codes for special purposes	0	0	0	0	1	0	0	0	0	0	2	0
Total	31,089		15,598		10,789		4,400		700		3,139	

Abbreviations: N = number of admissions; CNS = central nervous system

Table 70: The distribution of secondary causes of admissions (ICD-10) by diagnostic group ICCC-3

Secondary cause of admissions (ICD-10)	Hepatic tumours		Bone tumours		STS		Germ cells tumours		Other epithelial neoplasm		Other unspecified neoplasm		Overall diagnostic group	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Certain infectious and parasitic diseases	23	3	158	2	206	3	64	1	53	2	9	5	2,720	3
Neoplasms	102	11	1,328	19	1,554	20	1,238	21	739	22	40	23	12,501	14
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	18	2	242	4	360	5	138	2	54	2	11	6	4,413	5
Endocrine, nutritional and metabolic diseases	41	4	136	2	131	2	110	2	77	2	2	1	1,910	2
Mental and behavioural disorders	0	0	15	0	85	1	124	2	47	1	0	0	671	1
Diseases of the nervous system	2	0	79	1	80	1	158	3	41	1	2	1	2,009	2
Diseases of the eye and adnexa	0	0	8	0	47	1	26	0	11	0	0	0	636	1
Diseases of the ear and mastoid process	3	0	24	0	59	1	12	0	13	0	0	0	512	1
Diseases of the circulatory system	8	1	66	1	60	1	75	1	63	2	2	1	1,279	1
Diseases of the respiratory system	24	3	161	2	173	2	186	3	81	2	1	1	2,468	3
Diseases of the digestive system	46	5	197	3	154	2	105	2	115	3	3	2	2,107	2
Diseases of the skin and subcutaneous tissue	5	1	65	1	43	1	30	1	11	0	1	1	599	1
Diseases of the musculoskeletal system and connective tissue	12	1	1,316	19	1,314	17	430	7	166	5	1	1	7,328	8

Secondary cause of admissions (ICD-10)	Hepatic tumours		Bone tumours		STS		Germ cells tumours		Other epithelial neoplasm		Other unspecified neoplasm		Overall diagnostic group	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Diseases of the genitourinary system	40	4	85	1	104	1	112	2	46	1	4	2	1,142	1
Pregnancy, childbirth and the puerperium	1	0	12	0	19	0	11	0	63	2	0	0	284	0
Congenital malformations, deformations and chromosomal abnormalities	47	5	3	0	99	1	66	1	27	1	0	0	1,104	1
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	213	23	358	5	798	10	273	5	282	8	35	20	12,952	14
Injury, poisoning and certain other consequences of external causes	16	2	130	2	101	1	72	1	36	1	3	2	1,357	1
External causes of morbidity and mortality	28	3	290	4	255	3	197	3	54	2	7	4	2,901	3
Factors influencing health status and contact with health services	283	31	2,169	32	2,301	29	2,416	41	1,423	42	56	32	31,904	35
Codes for special purposes	0	0	0	0	0	0	0	0	0	0	0	0	3	0
Total causes	914	100	6,842	100	7,944	100	5,856	100	3,402	100	177	100	90,850	100

Abbreviations: N = number of admissions; STS = soft tissue sarcoma

8.3 Duration to first admission after completion of cancer treatment

8.3.1 The median time of admission after treatment completion by cause of admission and age at diagnosis

The aim of this subset analysis was to identify the group with the earliest admission for specific causes, given their age at diagnosis and type of cancer. The results of this section could help healthcare providers and planners to predict the period likely for each diagnostic group to return to hospital after recovering from cancer.

The follow-up time was calculated from the date of treatment completion until the date of first admission for certain causes, or censored at the date of death, last seen in the cancer register or end of the study period (31st December 2011) whichever occurred first.

The median time of first admission was subdivided by age at diagnosis (0-14, 15-29 and for all ages 0-29 years), this was carried out based on clinical interest in understanding whether there were differences in time to first admission by age group, given the potential differences in treatment management (paediatric vs young adults setting). The time at risk was estimated for cases with at least one hospital admission after completion of their initial treatment, and summary estimates were calculated for the median and interquartile range to first admission.

Any causes with less than five cases for one of the age groups was eliminated from the analysis, and the time to first admission was analysed for any one age group with a sufficient number of cases (more than five). The significance of the difference was estimated using the Mann-Whitney test (as detailed in Chapter 4).

8.3.1.1 Certain infectious and parasitic diseases

Out of 2,304 cancer survivors that were followed up after initial treatment completion, 223 (10%) had at least one admission for certain infectious diseases and contributed 347 person-years of follow-up time. This was broken down by age group with 133 (14%) out of 922 childhood survivors and 90 (6.5%) out of 1,382 TYA survivors, who contributed 143 and 205 person-years of follow-up time, respectively. Children were admitted earlier than TYAs for the majority of diagnostic groups, except for STS where the median was 1 year and 0.67 years for children and TYAs, respectively (Figure 65). The difference was significantly different among cases with leukaemia (median=138 days and 310 days for children and TYAs, respectively, *P*-value= 0.003).

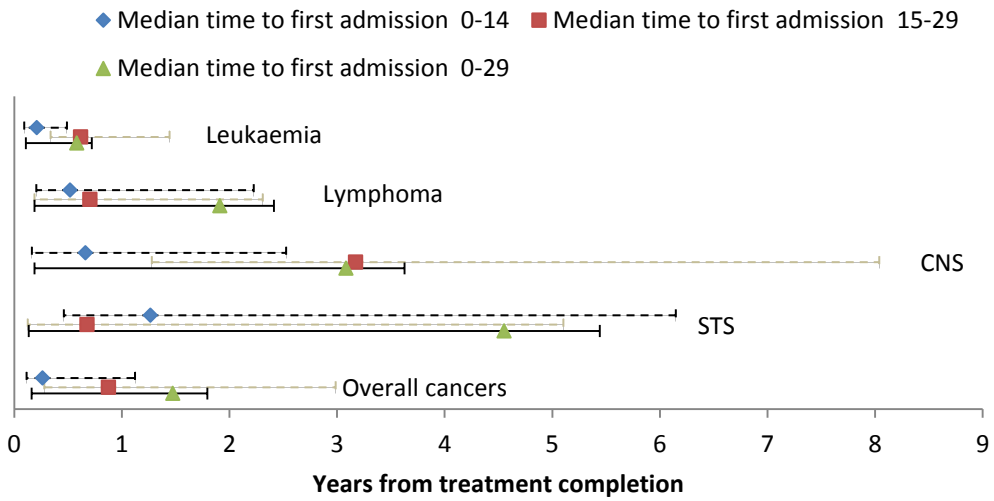

Figure 65: Median time to first admission for certain infectious and parasitic diseases by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.2 Neoplasms

Out of 2,304 cancer survivors that were followed up after initial treatment completion, 599 (26%) had at least one admission for neoplasms (disease of the recurrence of malignancy or subsequent primaries combined) and contributed to 812 person-years of follow-up time. This was broken down by age group with 310 (34%) out of 922 childhood survivors and 289 (21%) out of 1,382 TYA survivors, who contributed to 277 and 535 person-years of follow-up time, respectively. Neoplasm admissions were earlier among children than in TYAs (*P*-value <0.001), except for germ cell tumours, but that was not statistically significant. The difference was significant among cases with leukaemia having a median of 79 days compared with 237 days for children and TYAs, respectively (*P*-value <0.001) (Figure 66). The difference was also significant among lymphoma cases (median=78 days and 361 days for children and TYAs, respectively, *P*-value<0.001) and CNS (median=105 and 380 days for children and TYAs, respectively, *P*-value=0.007).

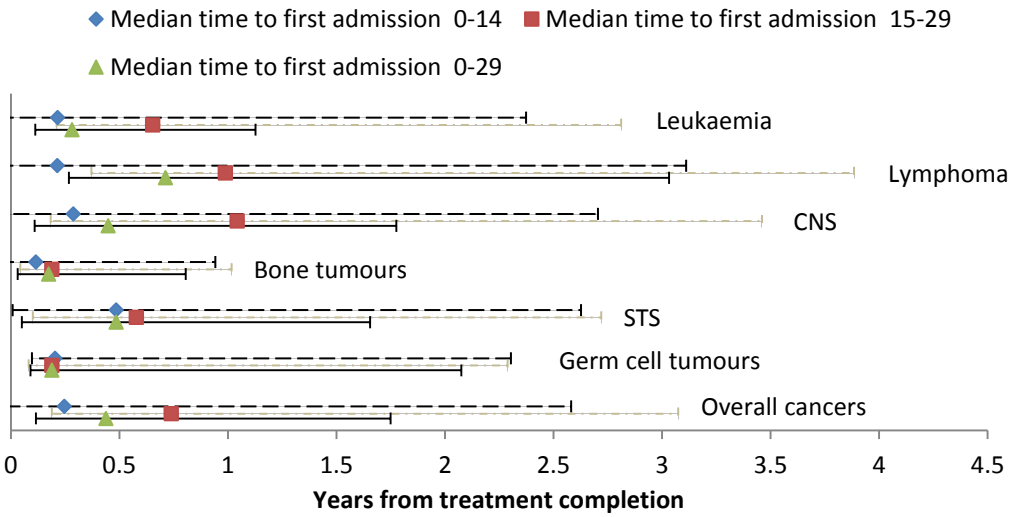

Figure 66: Median time to first admission for neoplasms by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.3 Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism

Out of 2,304 cancer survivors that were followed up after treatment completion, 183 (8%) had at least one admission for diseases of the blood, contributing to 234 person-years of follow-up time. This was broken down by age group with 102 (11%) out of 922 childhood survivors and 81 (6%) out of 1,382 TYA survivors, contributing to 89 and 144 person-years of follow-up time, respectively (Figure 67). Children were more likely to be admitted earlier than TYAs for all cancers (median=67 days and 239 days respectively, *P*-value <0.001) except for STS. The difference was statistically significant among cases surviving leukaemia (median= 63.55 and 124 days for children and TYAs, respectively, *P*-value=0.015) and lymphoma (median= 53 and 320 days, *P*-value=0.001, respectively). Children with lymphoma had the shortest time at risk compared with other diagnostic groups, while TYAs had the shortest time at risk when surviving from STS.

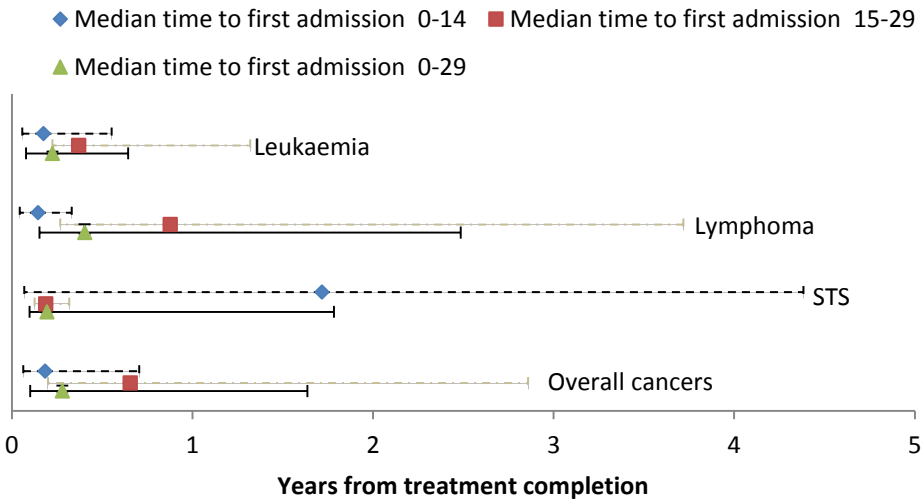

Figure 67:Median time to first admission for diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.4 Endocrine nutritional and metabolic diseases

Out of 2,304 cancer survivors that were followed up after treatment completion, 179 (8%) had at least one admission for endocrine nutritional and metabolic diseases, which contributed to 596 person-years of follow-up time. This was broken down by age group with 86 (9%) out of 922 childhood survivors and 93 (7%) out of 1,382 TYA survivors, contributing to 241 and 355 person-years of follow-up time, respectively. Children were admitted significantly earlier than TYAs for endocrine-related complications (*P*-value= 0.016). The difference was significant among survival from leukaemia (median=136 days and 457 days for children and TYAs, respectively, *P*-value=0.036). Children surviving from leukaemia had the shortest time at risk compared with other diagnostic groups, while TYAs had the shortest time at risk when surviving from STS (Figure 68).

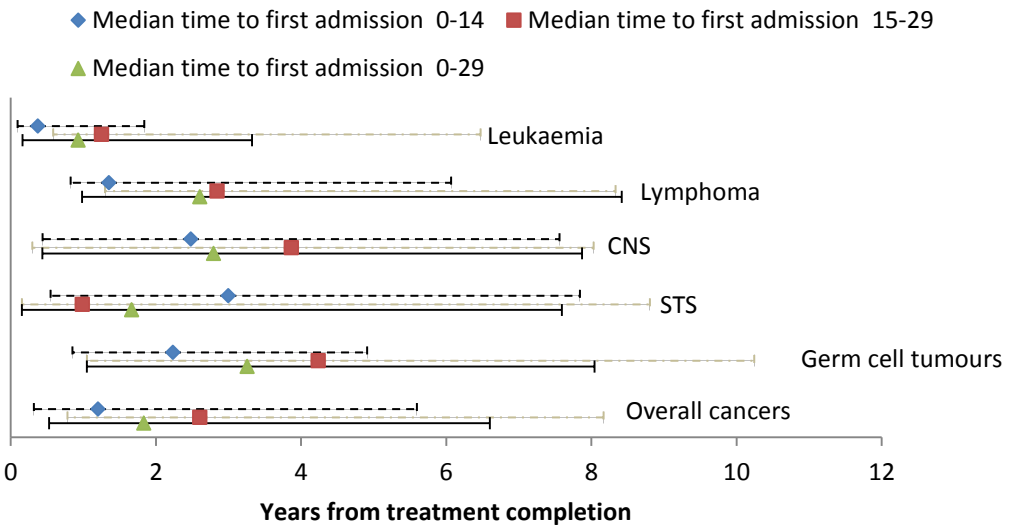

Figure 68: Median time to first admission for nutritional and metabolic diseases by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.5 Mental and behavioural disorders

Out of 2,304 cancer survivors followed up after treatment completion, 115 (8%) had at least one admission for mental and behavioural disorders, contributing to 511 person-years of follow-up time. This was broken down by age group with 31 (9%) out of 922 childhood survivors and 84 (7%) out of 1,382 TYA survivors, contributing to 136 and 375 person-years of follow-up years, respectively. TYAs were likely to be admitted earlier than children for mental disorders, except for STS (Figure 69). Children and TYAs surviving from CNS had the shortest median time to first admission for mental disorders (median=3 and 1 year/s for children and TYAs, respectively).

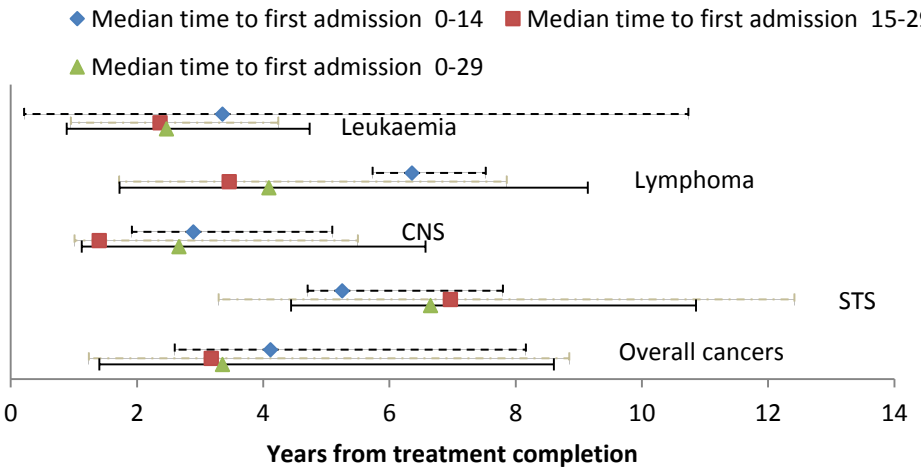

Figure 69: Median time to first admission for mental and behavioural disorders by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.6 Diseases of the nervous system

Out of 2,304 cancer survivors that were followed up after treatment completion, 143 (6%) had at least one admission for diseases of the nervous system, contributing to 420 person-years of follow-up time. This was broken down by age group with 61 (7%) out of 922 childhood survivors and 82 (6%) out of 1,382 TYA survivors, contributing to 161 and 259 person-years of follow-up time, respectively. Children experienced earlier admissions for diseases of the nervous system than TYAs for all cancers combined, while TYAs surviving from CNS had earlier admissions than children (median=2 and 1.4 years for children and TYAs, respectively) (Figure 70).

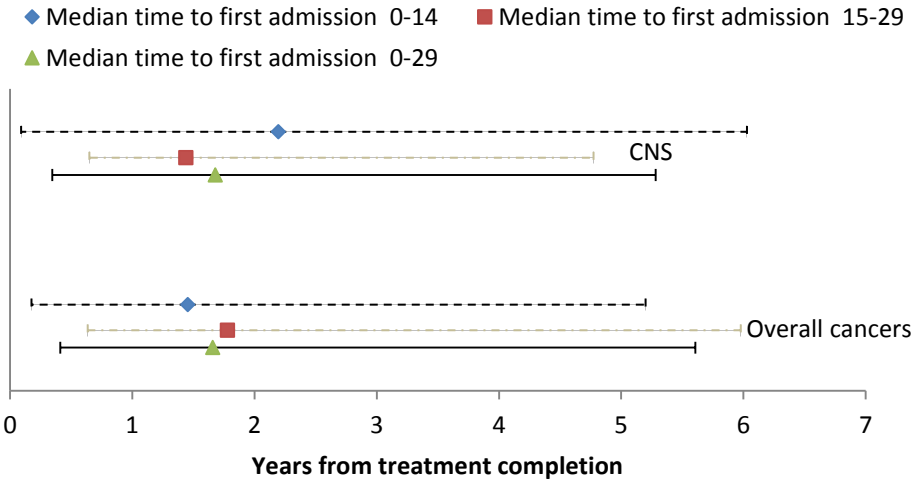

Figure 70: Median time to first admission for diseases of the nervous system by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.7 Diseases of the eye and adnexa

Out of 2,304 cancer survivors that were followed up after treatment completion, 70 (3%) had at least one admission for diseases of the eye and adnexa, which contributed to 217 person-years of follow-up time. This was broken down by age group with 47 (5%) out of 922 childhood survivors and 23 (2%) out of 1,382 TYA survivors, contributing to 137 and 80 person-years of follow-up time, respectively. TYAs experienced earlier admissions for eye complications than children for overall cancers combined (median=2.5 and 1.6 years for children and TYAs, respectively), but not for CNS survivors (Figure 71).

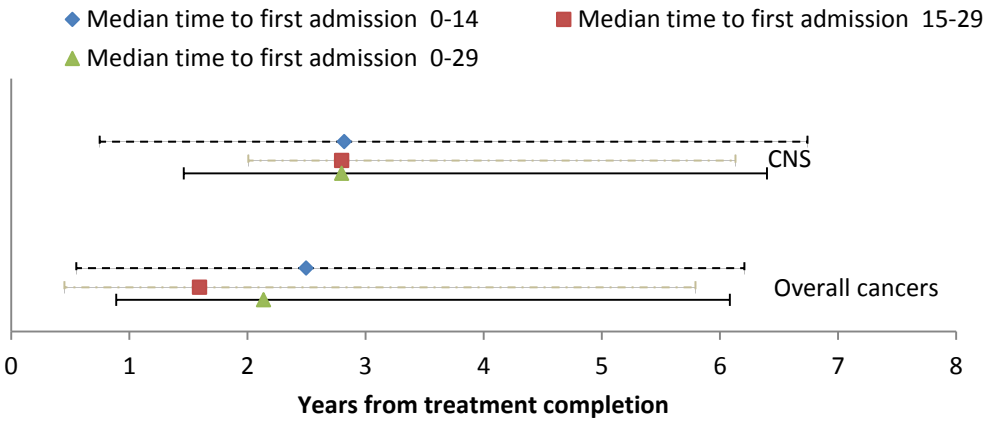

Figure 71: Median time to first admission for diseases of the eye and adnexa by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.8 Diseases of the ear and mastoid process

Out of 2,304 cancer survivors followed up after treatment completion, 43 (2%) had at least one admission for diseases of the ear and mastoid process, which contributed to 217 person-years of follow-up time. This was broken down by age group with 34 (4%) out of 922 childhood survivors and 9 (1%) out of 1,382 TYA survivors, contributing to 137 and 80 person-years follow-up time, respectively. Children surviving from leukaemia were admitted earlier for diseases of the ear than CNS survivors, where the median was 0.5 and 2 years, respectively (Figure 72).

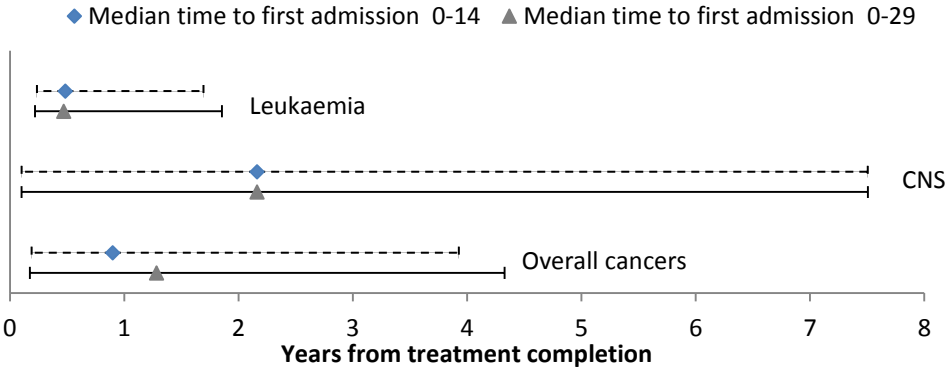

Figure 72:Median time to first admission for diseases of the ear and mastoid process by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.9 Diseases of the circulatory system

Out of 2,304 cancer survivors followed up after treatment completion, 115 (5%) had at least one admission for diseases of the circulatory system, which contributed to 397 person-years of follow-up time. This was broken down by age group with 44 (5%) out of

922 children survivors and 71 (5%) out of 1,382 TYA survivors, contributing to 137 and 260 person-years of follow-up time, respectively.

Children were admitted earlier than TYAs for circulatory diseases, except for leukaemia survivors where the median was significantly shorter for TYAs than for children, having less than a year (227 days) and four years respectively (*P*-value= 0.03) (Figure 73). Overall, lymphoma childhood survivors were admitted earlier than other diagnostic groups, while TYAs with leukaemia were admitted earlier than other diagnostic groups.

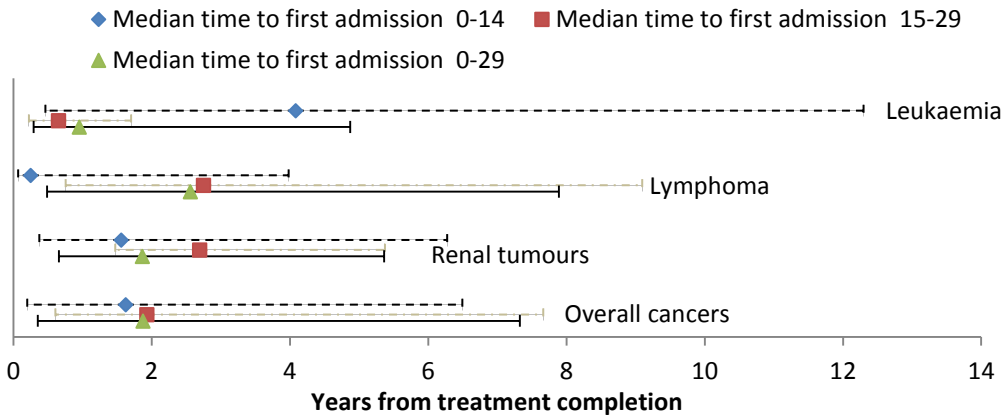

Figure 73: Median time to first admission for diseases of the circulatory system by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.10 Diseases of the respiratory system

Out of 2,304 cancer survivors that were followed up after treatment completion, 229 (12%) had at least one admission for diseases of the respiratory system, which contributed to 770 person-years of follow-up. This was broken down by age group with 101 (14%) out of 922 childhood survivors and 128 (10%) out of 1,382 TYA survivors, and contributed to 345 and 424 person-years of follow-up time, respectively. Children had shorter median times to first admission than TYAs, except for leukaemia, CNS, and STS with no significant differences observed (Figure 74).

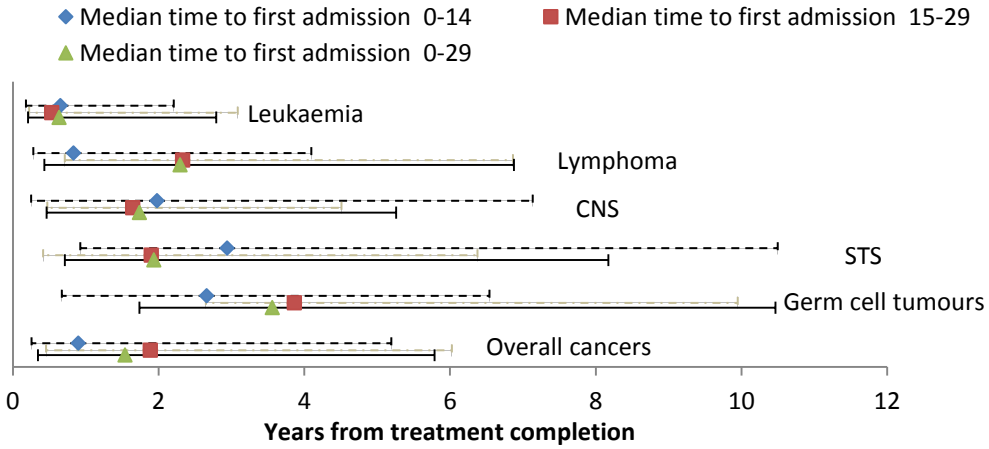

Figure 74: Median time to first admission for diseases of the respiratory system by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.11 Diseases of the digestive system

Out of 2,304 cancer survivors that were followed up after treatment completion, 209 (9%) had at least one admission for diseases of the digestive system, which contributed to 680 person-years of follow-up time. This was broken down by age group with 92 (10%) out of 922 childhood survivors and 117 (8%) out of 1,382 TYA survivors, and contributed to 278 and 402 person-years of follow-up time, respectively. Children had a shorter median time to admission than TYAs, where the medians were 1 and 2.5 years for children and TYAs, respectively (not significant) (Figure 75).

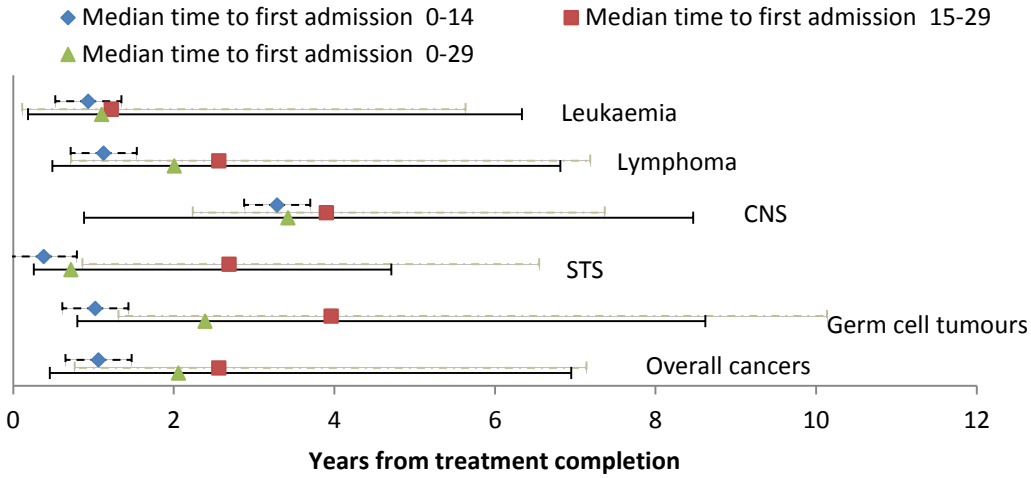

Figure 75: Median time to first admission for diseases of the digestive system by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.12 Diseases of the skin and subcutaneous tissue

Out of 2,304 cancer survivors followed up after treatment completion, 66 (3%) had at least one admission for diseases of the skin and subcutaneous tissue, contributing to 157 person-years. This was broken down by age group with 29 (3%) out of 922 childhood survivors and 37 (3%) out of 1,382 TYA survivors, contributing to 49 and 108 person-years of follow-up time, respectively. Children had significantly shorter median times to first admission compared with TYAs (median=252 days vs 752 days, respectively, *P*-value= 0.03) and this pattern was observed for all diagnostic groups except for lymphoma (Figure 76).

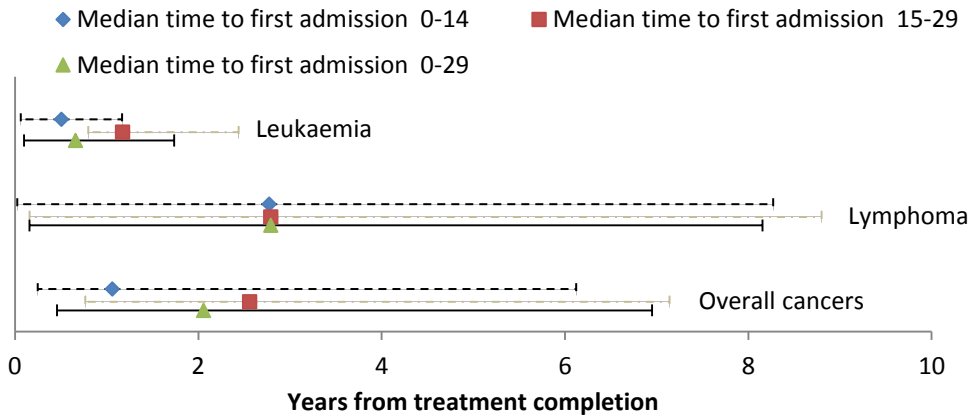

Figure 76: Median time to first admission for diseases of the skin and subcutaneous tissue by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.13 Diseases of the musculoskeletal system and connective tissue

Out of 2,304 cancer survivors that were followed up after treatment completion, 216 (9%) had at least one admission for diseases of the musculoskeletal system and connective tissue, which contributed to 385 person-years of follow-up time. This was broken down by age group with 125 (14%) out of 922 childhood survivors and 91 (7%) out of 1,382 TYA survivors, contributing to 133 and 252 person-years of follow-up time, respectively. Children had a significantly shorter median time at risk compared with TYAs (median=115 days and 368 days, respectively, P-value= <0.001) (Figure 77).

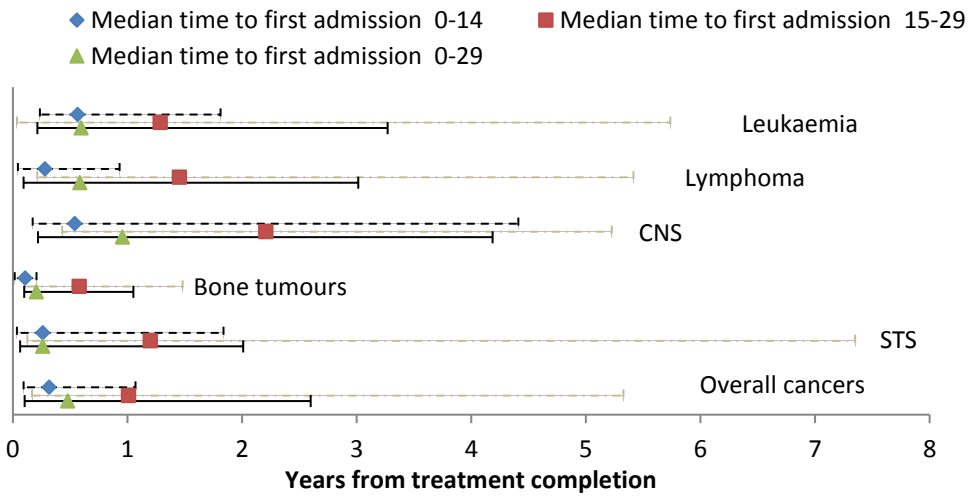

Figure 77: Median time to first admission for diseases of the musculoskeletal system and connective tissue by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.14 Diseases of the genitourinary system

Out of 2,304 cancer survivors followed up after treatment completion, 122 (5%) had at least one admission for diseases of the genitourinary system, which contributed to 359 person-years of follow-up time. This was broken down by age group with 40 (4%) out of 922 childhood survivors and 82 (6%) out of 1,382 TYA survivors, contributing to 108 and 251 person-years of follow-up time, respectively. Children had shorter median times at risk compared with TYAs, except for leukaemia (Figure 78).

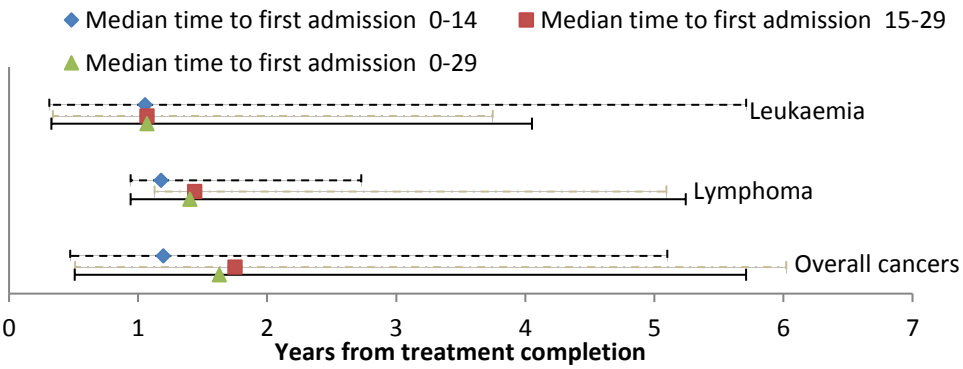

Figure 78: Median time to first admission for diseases of the genitourinary system by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.15 Pregnancy, childbirth and the puerperium

Out of 2,304 cancer survivors followed up after treatment completion, 77 (3%) had at least one admission for pregnancy, childbirth and the puerperium, which contributed to 316 person-years of follow-up time. This was broken down by age group with 8 (1%) out of 922 childhood survivors and 69 (5%) out of 1,382 TYA survivors, and contributed to 60 and 255 person-years of follow-up time, respectively. TYAs on average (median) were admitted earlier for pregnancy and puerperium related causes than children (medians of three and eight years, respectively, P-value= 0.001). The median time to first admission for pregnancy related conditions among TYAs (69 cases) was earlier among germ cell tumour survivors than lymphoma and CNS tumour survivors (Figure 79).

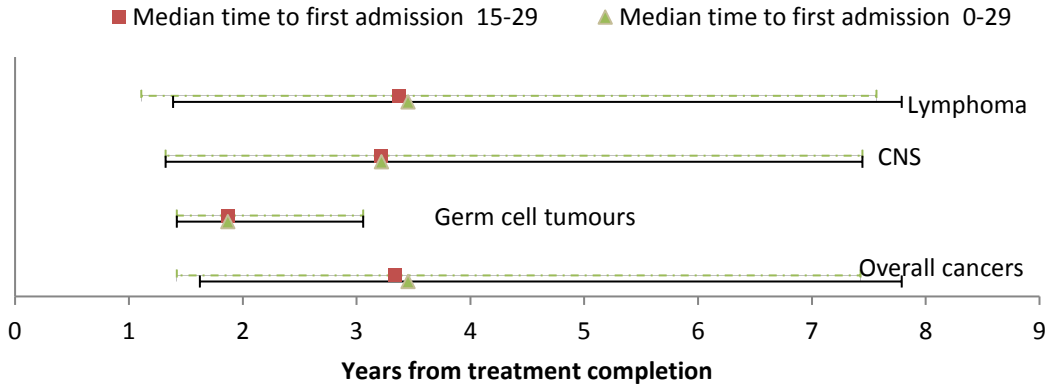

Figure 79: Median time to first admission for pregnancy childbirth and the puerperium by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.16 Congenital malformations, deformations and chromosomal abnormalities

Out of 2,304 cancer survivors followed up after treatment completion, 65 (3%) had at least one admission for congenital malformations, deformations and chromosomal abnormalities, which contributed to 142 person-years of follow-up time. This was broken down by age group into 45 (5%) out of 922 childhood survivors and 20 (1%) out of 1,382 TYA survivors, contributing to 111 and 31 person-years of follow-up time respectively. TYAs were admitted earlier than children for all groups except CNS tumours, however this was not significant (median=338 and 157 days for children and TYAs, respectively).

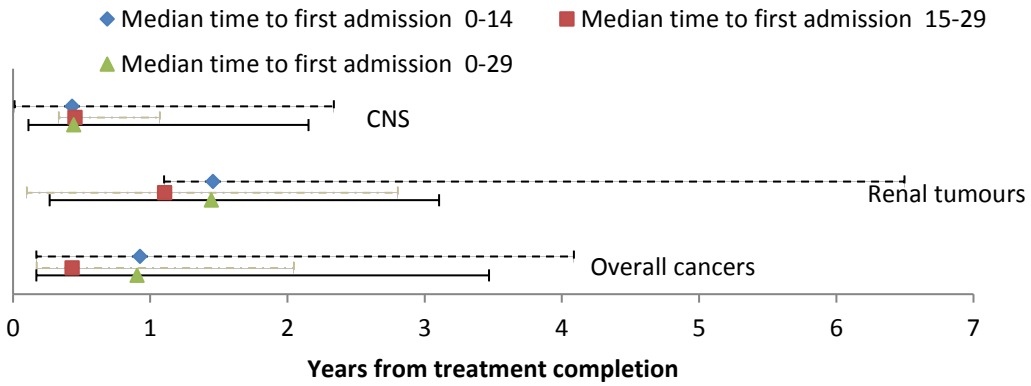

Figure 80: Median time to first admission for congenital malformations, deformations and chromosomal abnormalities by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.17 Symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified

Out of 2,304 cancer survivors followed up after treatment completion, 534 (23%) had at least one admission for causes classified as symptoms, signs and abnormal clinical and laboratory findings, which contributed to 1,098 person-years of follow-up time. This was broken down by age group with 289 (31%) out of 922 childhood survivors and 245 (18%) out of 1,382 TYA survivors, contributing to 412 and 687 person-years of follow-up time respectively. Children on average (median) were admitted earlier than TYAs (median = less than one year and almost two years, respectively, *P*-value <0.001) (Figure 81), except for renal tumours but was not significant.

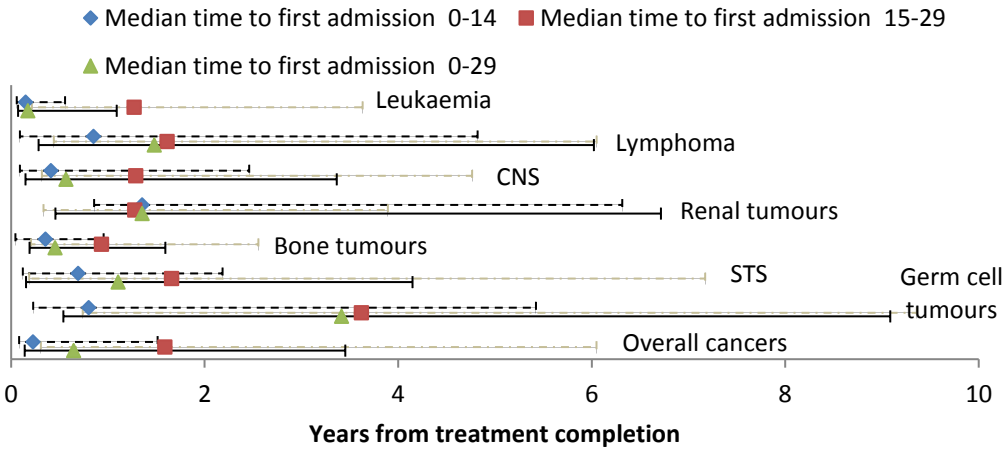

Figure 81: Median time to first admission for symptoms signs and abnormal clinical and laboratory findings not elsewhere classified by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.18 Injury, poisoning and certain other consequences of external causes

Out of 2,304 cancer survivors followed up after treatment completion, 142 (6%) had at least one admission for causes classified as injury, poisoning and certain other consequences of external causes, contributing to 397 person-years of follow-up time. This was broken down by age group into 59 (6%) out of 922 childhood survivors and 83 (6%) out of 1,382 TYA survivors, and contributed to 154 and 243 person-years of follow-up time, respectively. Children had shorter median times at risk compared with TYAs except for lymphoma and CNS tumour survivors (Figure 82). The difference was significant for leukaemia survivors (median=119 and 460 days for children and TYAs, respectively).

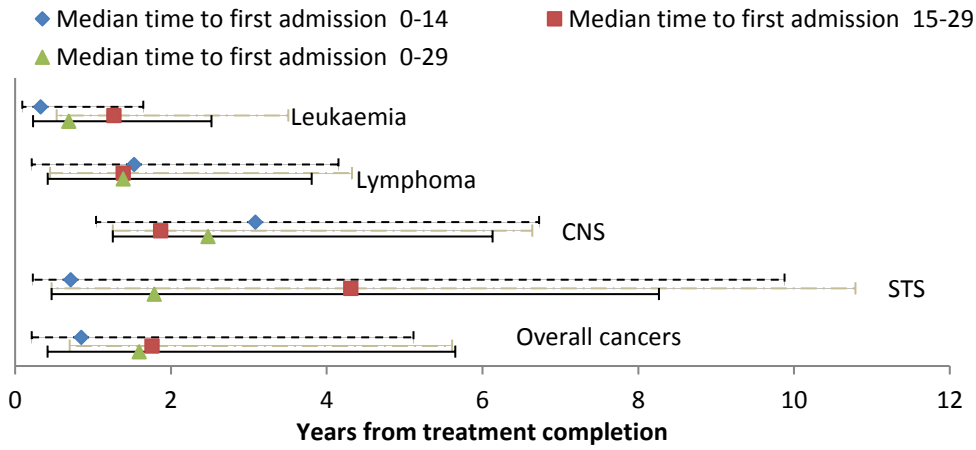

Figure 82: Median time to first admission for injury poisoning and certain other consequences of external causes by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.19 External causes of morbidity and mortality

Out of 2,304 cancer survivors that were followed up after treatment completion, 272 (12%) had at least one admission for causes classified as external causes of morbidity and mortality, and contributed to 671 person-years of follow-up time. This was broken down by age group with 127 (14%) out of 922 childhood survivors and 145 (10%) out of 1,382 TYA survivors, contributing to 253 and 418 person-years of follow-up time, respectively. Children were admitted earlier (median less than a year and two years for children and TYAs, respectively, *P*-value= 0.002) than TYAs except for those with bone tumours and STS, but this was not significant (Figure 83).

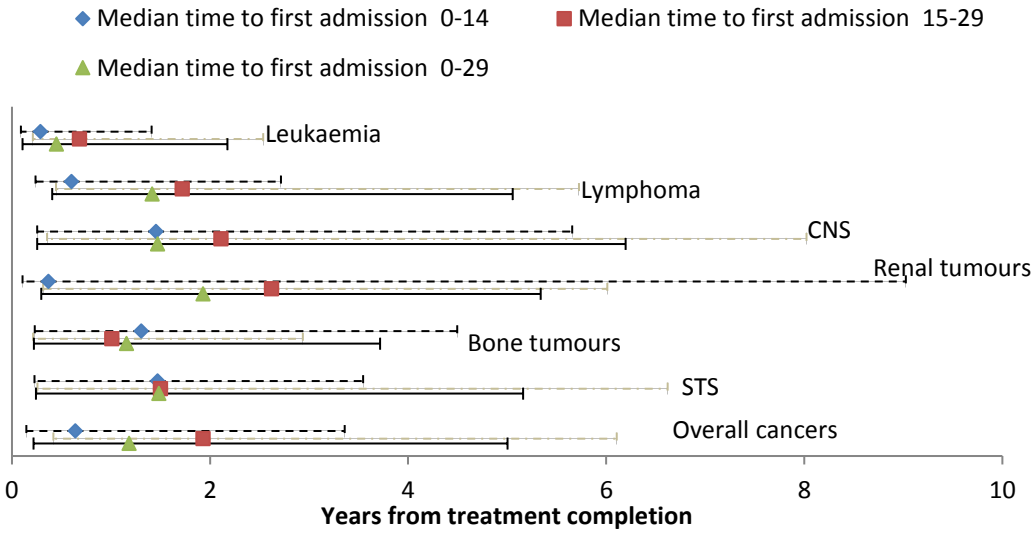

Figure 83:Median time to first admission for external causes of morbidity and mortality by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.20 Factors influencing health status and contact with health services

Out of 2,304 cancer survivors followed up after treatment completion, 1,218 (53%) had at least one admission for causes classified as factors influencing health status and contact with health services, which contributed to 2,484 person-years of follow-up time. This was broken down by age group into 592 (64%) out of 922 childhood survivors and 626 (45%) out of 1,382 TYA survivors, contributing to 694 and 1,789 person-years of follow-up time, respectively. Children had shorter median times to first admission for the majority of diagnostic groups compared with TYAs (median 0.30 and 1.56 years for children and TYA, respectively, *P*-value= <0.001) (Figure 84).

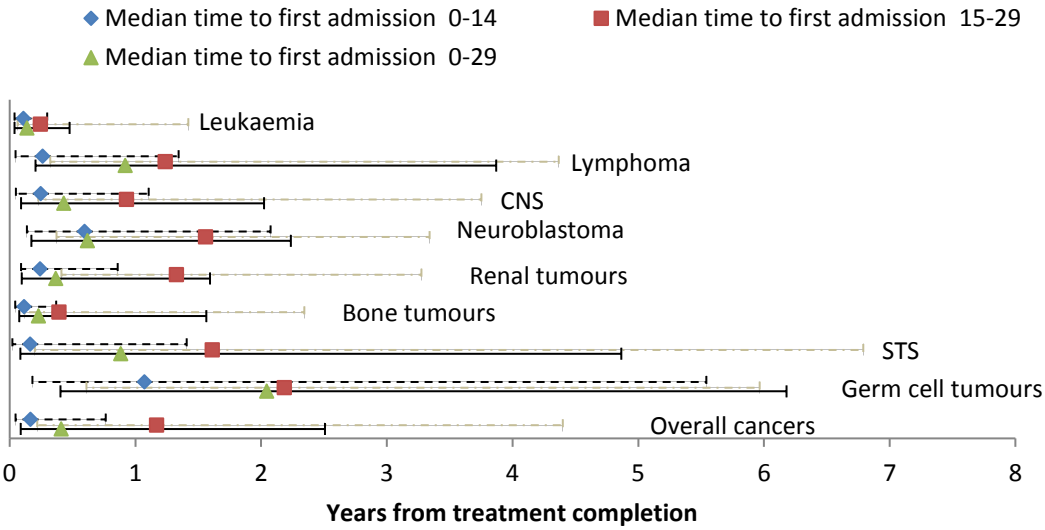

Figure 84: Median time to first admission for first admission to factors influencing health status and contact with health services by age at diagnosis, diagnostic group after initial treatment completion

8.3.1.21 Total admissions

Out of 2,304 cancer survivors followed up after treatment completion, 1,723 (75%) had at least one hospital admission, contributing to 2,553 person-years of follow-up time. This was broken down by age group into 776 (84%) out of 922 childhood survivors and 947 (69%) out of 1,382 TYA survivors, contributing to 687 and 1,866 person-years, respectively. For all causes of admissions combined, children experienced a shorter time to first admission compared with TYAs (median= 0.17 and 1.17 years for children and TYAs, respectively, *P*-value= <0.001). The shortest admission times overall were among leukaemia and bone tumour survivors. Furthermore, the time to first admission for these two diagnostic groups was significantly shorter among children than TYAs (*P*-value= <0.001 and 0.005 respectively) (Figure 85).

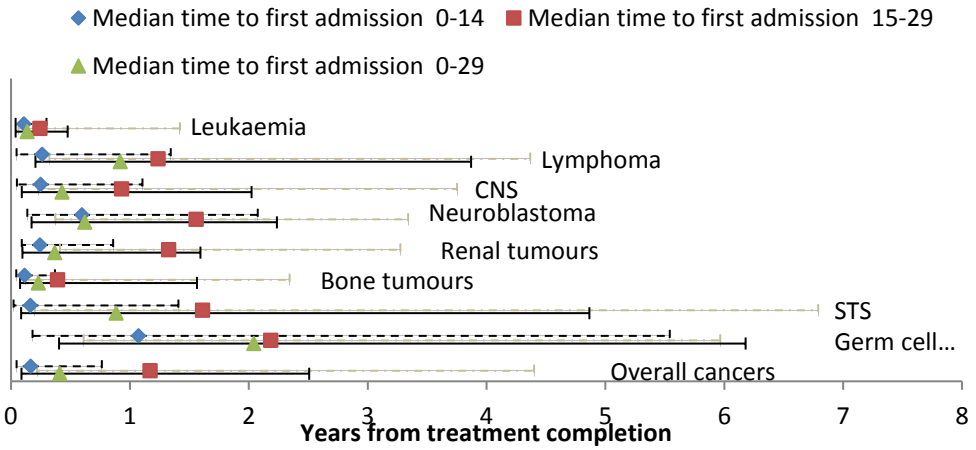

Figure 85: Median time to first admission for first admission to overall cases in combined by age at diagnosis, diagnostic group after initial treatment completion

8.4 Excess hospitalisation rate compared with background population

In this section, the health burden after completion of cancer treatment in terms of rate of admission among the cancer cohort compared with the background population was analysed. Among the age-sex and admissions year matched background population, there was 2,236,680 individuals aged 0-45 years and were admitted at least once to hospital and contributed to over than 6 million admissions. The standardised mortality ratio technique was used to estimate the excess standardised hospitalisation ratio (SHR) among cancer cohort. For the background population, the rate was calculated by dividing the total number of admissions (first admission per cause) by single age, sex and mid-year population estimates. The rate of admissions among matched attained age, sex and year of admission for the background population was used to standardise rate among cancer cohort (more detail in Section 4.7).

The follow-up years (1997-2011) among the cancer cohort was from the date of treatment completion until the date of the first admission (primary or secondary diagnosis at admission) and censored at date of death, loss of follow-up or end of the study period (31stDecember 2011). The SHR was subdivided by age at diagnosis, gender and cancer types. Late effects of cancer and its treatment were identified as five-year survival from date of diagnosis [15, 24, 101, 140, 149], however, use of this method would illuminate a number of admissions that occurred after treatment completion and before the five-year cut-off point, hence underestimating the burden of health preceding the date of treatment completion. 12,474 admissions were found in the current analysis that occurred after treatment completion, but within five years of the date of diagnosis.

The rate of admission was higher among the cancer cohort compared with the background population for all admission diagnoses combined (SHR=2.37, 95% CI:2.26-2.49), except for those due to pregnancy (SHR= 0.9, 95% CI:0.7-1.2) (Table 71). The highest SHR was for admissions due to ‘diseases of the blood’, followed by ‘neoplasms’ and then ‘endocrine and metabolic diseases’ including diabetes, having SHR=55.8, 49.6 and 32.1, respectively.

Overall, leukaemia survivors had the highest SHR (SHR=10.0, 95%CI:9.1-11.0), whilst germ cell tumour survivors had the lowest SHR compared with other diagnostic groups, adjusting for the background population (SHR=1.52, 95%CI:1.37-1.69) (Figure 86, Table 71 and Table 73). Leukaemia survivors had the highest SHR for ‘certain infectious diseases’, ‘neoplasms’, ‘diseases of the blood’ and ‘respiratory diseases’ compared with other diagnostic groups, having SHR=44.4, 144.7, 139.9 and 12.3 respectively (Figure 86 and Table 71).

CNS tumour survivors had the highest SHR for ‘mental and behavioural disorders’ and ‘diseases of the nervous system’ compared with other diagnostic groups (SHR=23.4 and 70.9, respectively) (Figure 86 and Table 71). While, renal tumour cases had the highest SHR for ‘circulatory system diseases’ (SHR=41.67, 95%CI:24.7-70.4) followed by leukaemia survivors (SHR=22.4 95% CI:15.8-31.7) (Figure 86 and Table72)

Children had a higher SHR than TYAs for all causes combined (SHR=6.94 and 1.68 respectively, Figure 87). However, admissions for ‘endocrine and metabolic diseases’ were higher among TYAs than children (SHR=10.69 and 15.29 for children and TYAs, respectively). The difference in the hospitalisation rate was significant for ‘neoplasms’, ‘diseases of the blood’ and ‘circulatory diseases’ among children and TYAs, where the rate was three- to five-fold higher among children (Figure 87).

For all causes of admissions combined, males had a higher SHR than females after completion of cancer treatment (SHR=2.81 and 2.04, respectively, Figure 88). However, that was mainly for ‘neoplasms’, ‘diseases of the blood’, and ‘diseases of the nervous system’. While for the other causes, females had a higher SHR, such as ‘endocrine and metabolic diseases’, ‘mental and behavioural diseases’ and ‘diseases of the circulatory system’ than males.

Table 71: Standardised hospitalisation ratio after completion of treatment by primary cancer type and cause of admissions (ICD-10)

Causes of admissions (ICD-10)	All cancers				Leukaemia				Lymphoma				CNS			
	N	SHR	LCI	UCI	N	SHR	LCI	UCI	N	SHR	LCI	UCI	N	SHR	LCI	UCI
All diagnosis combined*	1,723¥	2.37	2.26	2.49	438	10	9.1	11	388	1.5	1.3	1.6	257	3.5	3.1	3.9
Certain infectious and parasitic diseases	223	16.5	14.5	18.8	97	44.4	36.4	54.2	47	17.1	12.9	22.8	26	16.5	11.2	24.2
Neoplasms	598	49.6	45.8	53.8	193	144.7	125.6	166.6	142	35.9	30.5	42.3	97	85.4	70	104.2
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	183	55.8	48.3	64.6	69	139.9	110.5	177.1	45	45.9	34.3	61.5	22	60.5	39.8	91.8
Endocrine, nutritional and metabolic diseases	179	32.1	27.8	37.2	40	44.8	32.8	61	39	23.7	17.3	32.4	43	69.5	51.6	93.8
Mental and behavioural disorders	115	13.7	11.4	16.5	16	16.6	10.2	27.2	36	15	10.8	20.8	18	23.4	14.8	37.2
Diseases of the nervous system	142	14.1	12	16.6	10	6.7	3.6	12.4	15	5.1	3.1	8.5	74	70.9	56.5	89
Diseases of the eye and adnexa	70	9.9	7.8	12.5	12	9.9	5.6	17.5	4	2.3	0.9	6.2	35	44.1	31.7	61.4
Diseases of the ear and mastoid process	43	6.5	4.9	8.8	15	10.4	6.3	17.2	5	4.3	1.8	10.4	8	9	4.5	18
Diseases of the circulatory system	114	7.9	6.6	9.5	32	22.4	15.8	31.7	28	6.5	4.5	9.4	13	10.8	6.3	18.7
Diseases of the respiratory system	226	6.7	6	7.6	83	12.2	9.9	15.2	66	7.1	5.5	9	28	6.5	4.5	9.4
Diseases of the digestive system	209	2.3	2	2.7	55	3.8	2.9	5	60	2.5	1.9	3.2	31	3.3	2.3	4.6
Diseases of the skin and subcutaneous tissue	66	3.1	2.5	4	26	9.7	6.6	14.3	13	2.2	1.3	3.7	9	4.3	2.3	8.4
Diseases of the musculoskeletal system and connective tissue	216	6.4	5.6	7.3	34	8	5.7	11.2	55	5.7	4.4	7.5	30	9.7	6.8	13.9

Causes of admissions (ICD-10)	All cancers				Leukaemia				Lymphoma				CNS			
	N	SHR	LCI	UCI	N	SHR	LCI	UCI	N	SHR	LCI	UCI	N	SHR	LCI	UCI
Diseases of the genitourinary system	121	3.2	2.7	3.8	29	5.3	3.7	7.7	27	2.2	1.5	3.3	11	2.6	1.4	4.7
Pregnancy, childbirth and the puerperium	77	0.9	0.7	1.2	10	0.8	0.4	1.5	37	1.1	0.8	1.5	13	1.3	0.8	2.2
Congenital malformations, deformations and chromosomal abnormalities	64	11.6	9.1	14.8	14	10.5	6.2	17.8	3	2.8	0.9	8.7	20	25.8	16.7	40
Symptoms, signs and abnormal clinical and laboratory findings not elsewhere classified	531	7.5	6.9	8.1	192	22.9	19.9	26.4	112	5.2	4.3	6.2	92	12.3	10	15
Injury, poisoning and certain other consequences of external causes	142	10.1	8.6	11.9	47	18.7	14.1	24.9	30	10.7	7.5	15.3	18	10.8	6.8	17.1
Factors influencing health status and contact with health services	1,263	32.2	30.4	34	361	88.6	79.9	98.3	279	18.1	16.1	20.3	196	48	41.8	55.3

Abbreviations: N = observed number of cases; SHR = standardised hospital ratio; LCI = 95% lower confidence interval; ULI = 95% upper confidence interval; STS = soft tissue sarcoma

* not a total of all admissions as each survivor could be admitted more than once for different causes.

¥ total of all cases with admissions after treatment completion.

Table 72: Standardised hospitalisation ratio after completion of treatment by primary cancer type and cause of admissions (ICD-10)

Causes of admissions ICD-10	Neuroblastoma				Renal tumours				Bone tumours			
	N	SHR	LCI	UCI	N	SHR	LCI	UCI	N	SHR	LCI	UCI
All diagnosis combined*	48	4.3	3.3	5.7	68	4.6	3.6	5.8	85	3.9	3.2	4.9
Certain infectious and parasitic diseases	4	4.5	1.7	11.9	6	5.3	2.4	11.9	11	25	13.8	45.1
Neoplasms	14	111.1	65.8	187.6	21	63.7	41.5	97.7	31	74.5	52.4	106
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	3	36.8	11.9	114	6	39.4	17.7	87.6	8	68	34	136
Endocrine, nutritional and metabolic diseases	4	39.2	14.7	104.5	7	34.2	16.3	71.7	7	35.5	16.9	74.4
Mental and behavioural disorders	2	31.7	7.9	126.7	0	NA	NA	NA	2	5.9	1.5	23.6
Diseases of the nervous system	3	13.9	4.5	43.2	5	13	5.4	31.4	8	22.7	11.4	45.5
Diseases of the eye and adnexa	2	8.7	2.2	34.8	1	2.8	0.4	20	2	8.8	2.2	35.2
Diseases of the ear and mastoid process	3	6.2	2	19.1	2	3.1	0.8	12.6	1	6.6	0.9	46.9
Diseases of the circulatory system	2	17.3	4.3	69	14	41.7	24.7	70.4	4	7.6	2.8	20.2
Diseases of the respiratory system	7	4	1.9	8.3	14	5.6	3.3	9.5	13	10.8	6.3	18.6
Diseases of the digestive system	3	1.5	0.5	4.5	9	2.7	1.4	5.2	6	1.9	0.8	4.1
Diseases of the skin and subcutaneous tissue	1	3.7	0.5	26.4	2	3.6	0.9	14.5	4	4.8	1.8	12.7
Diseases of the musculoskeletal system and connective tissue	10	30.8	16.6	57.2	17	24.5	15.2	39.4	17	14.2	8.8	22.9
Diseases of the genitourinary system	4	7	2.6	18.8	9	7.5	3.9	14.4	7	4.4	2.1	9.2
Pregnancy, childbirth and the puerperium	0	NA	NA	NA	1	0.6	0.1	4.2	4	0.9	0.3	2.4
Congenital malformations, deformations and chromosomal abnormalities	4	14.1	5.3	37.4	12	26.6	15.1	46.8	1	6.3	0.9	44.7
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	9	6.4	3.3	12.3	19	7.7	4.9	12	20	7.8	5	12.1
Injury, poisoning and certain other consequences of external causes	3	3.2	1	10.1	7	6.2	2.9	12.9	1	2.5	0.4	18
Factors influencing health status and contact with health services	34	62.5	44.6	87.4	53	45.4	34.7	59.4	66	44.9	35.2	57.1

Abbreviations: N = observed number of cases; SHR = standardised hospital ratio; LCI: 95% lower confidence interval; ULI= 95% upper confidence interval; STS = soft tissue sarcoma; NA = not applicable * not a total of all admissions as each survivors could be admitted more than once for different causes.

Table 73: Standardised hospitalisation ratio after completion of treatment by primary cancer type and cause of admissions (ICD-10)

Causes of admissions ICD-10	Soft tissue sarcomas				Germ cell tumours			
	N	SHR	LCI	UCI	N	SHR	LCI	UCI
All diagnosis combined*	126	1.8	1.5	2.2	301	1.3	1.2	1.5
Certain infectious and parasitic diseases	14	11.9	7.1	20.1	15	4.6	2.8	7.6
Neoplasms	44	40.6	30.2	54.6	48	13.4	10.1	17.8
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	12	41.8	23.7	73.6	15	19.4	11.7	32.2
Endocrine, nutritional and metabolic diseases	14	29.7	17.6	50.1	24	17.2	11.5	25.7
Mental and behavioural disorders	13	19.1	11.1	32.9	28	9.4	6.5	13.6
Diseases of the nervous system	10	11.8	6.3	21.9	17	6.3	3.9	10.1
Diseases of the eye and adnexa	4	7	2.6	18.7	9	4.7	2.4	9
Diseases of the ear and mastoid process	5	10.2	4.3	24.6	3	2.4	0.8	7.4
Diseases of the circulatory system	7	6	2.9	12.6	12	2.3	1.3	4.1
Diseases of the respiratory system	23	7.2	4.8	10.8	29	2.9	2	4.2
Diseases of the digestive system	12	1.7	1	3	32	1.3	0.9	1.8
Diseases of the skin and subcutaneous tissue	4	2.4	0.9	6.4	6	0.9	0.4	1.9
Diseases of the musculoskeletal system and connective tissue	25	9.6	6.5	14.1	25	2.1	1.4	3.2
Diseases of the genitourinary system	12	3.6	2	6.4	20	2.3	1.5	3.5
Pregnancy, childbirth and the puerperium	6	0.7	0.3	1.5	6	0.7	0.3	1.6
Congenital malformations, deformations and chromosomal abnormalities	5	11.3	4.7	27.3	5	5.2	2.2	12.6
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	34	5.6	4	7.8	46	2.2	1.7	3
Injury, poisoning and certain other consequences of external causes	13	11.6	6.7	20	19	5.7	3.6	8.9
Factors influencing health status and contact with health services	92	23.9	19.4	29.3	171	20	17.2	23.3

Abbreviations: N = observed number of cases; SHR = standardise hospital ratio; LCI: 95% lower confidence interval; ULI= 95% upper confidence interval; STS = soft tissue sarcoma; NA = not applicable

* not a total of admissions as each survivor admitted more than once for different causes

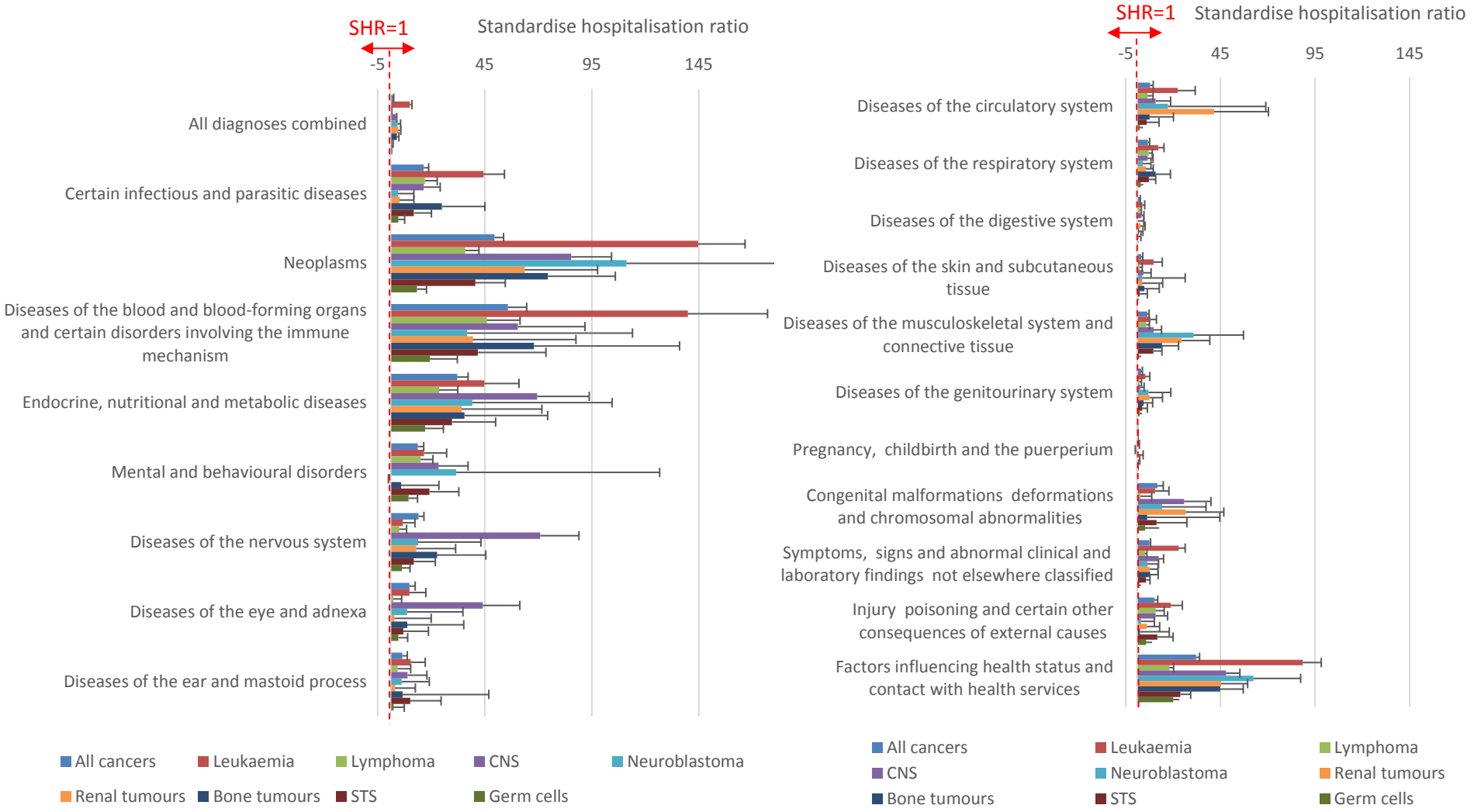

Figure 86: Standardised hospitalisation ratio with 95% confidence interval after treatment completion by cancer type at diagnosis and cause of admission (ICD-10)

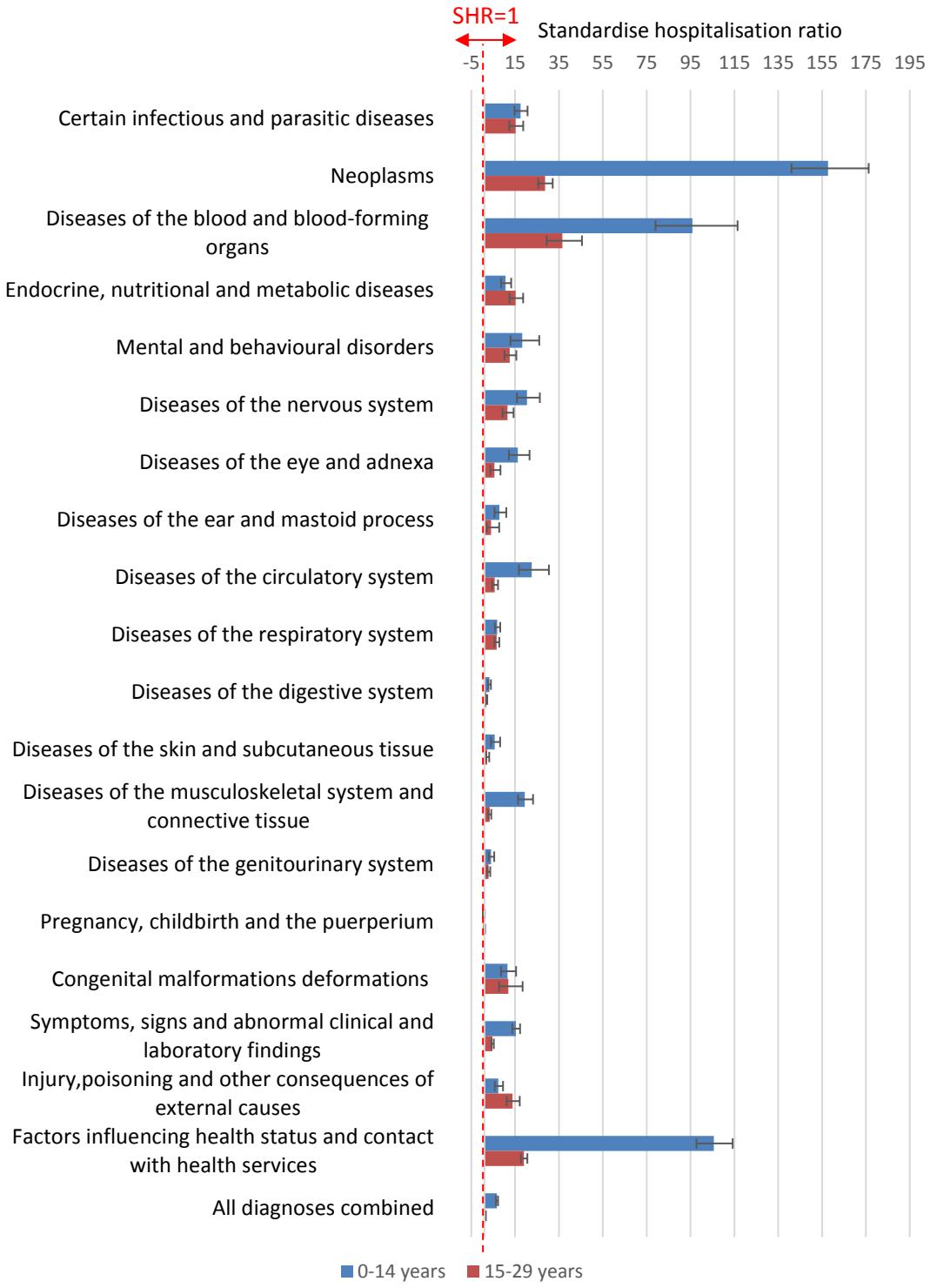

Figure 87: Standardised hospitalisation ratio with 95% confidence interval after treatment completion by age at diagnosis and cause of admission (ICD-10)

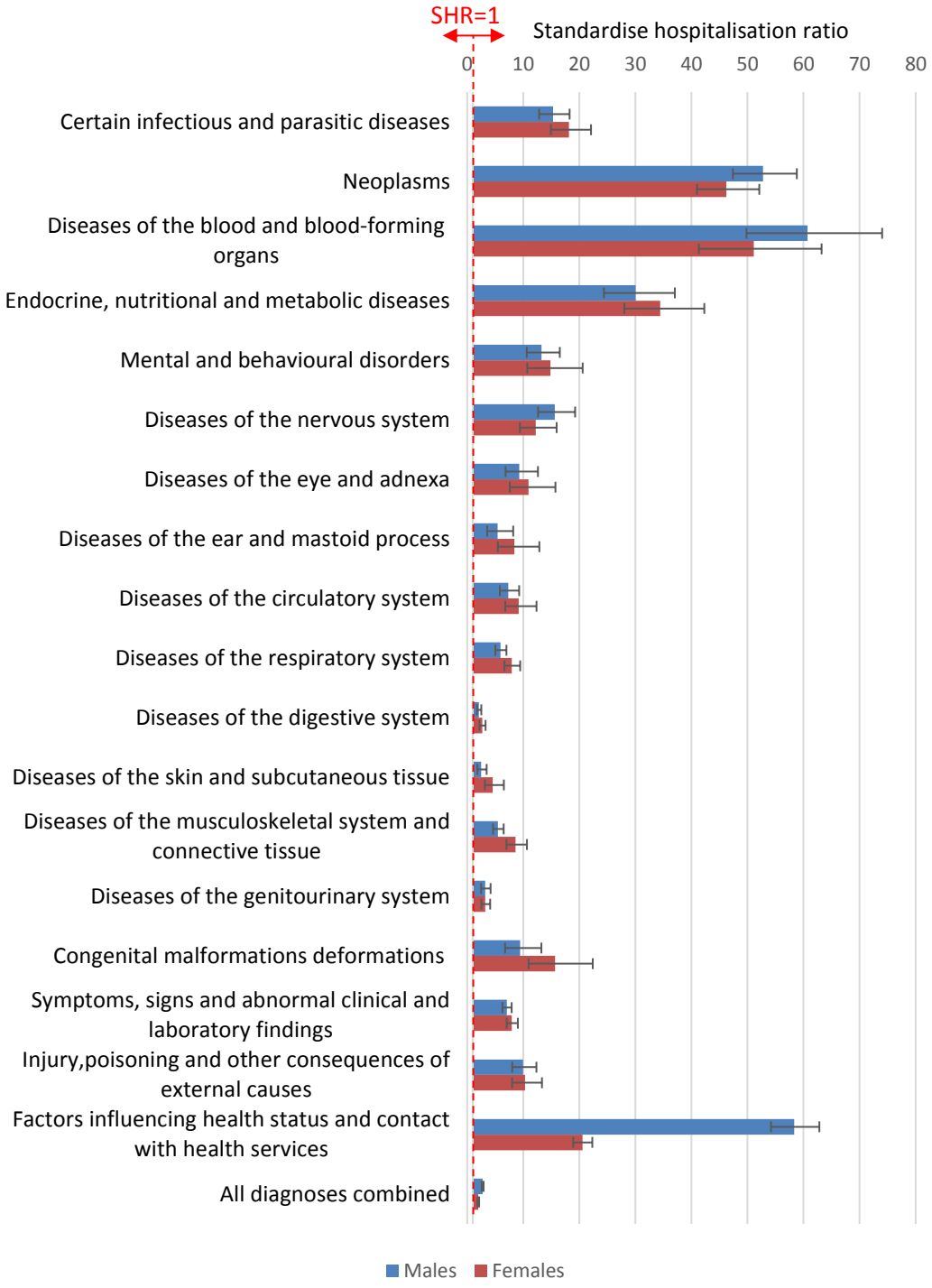

Figure 88: Standardised hospitalisation ratio with 95% confidence interval after treatment completion by gender and cause of admissions (ICD-10)

8.5 Summary

Morbidities that lead to hospitalisation were classified using primary and secondary diagnoses, in HES some causes always reported the main diagnosis while others did not. Therefore, the patterns of admission were assessed using primary and secondary diagnosis to ensure consistency in identifying common causes, without ignoring minor causes. Using both diagnoses (primary and secondary) 'neoplasms' were consistently the commonest reason for admission, followed by causes classified as 'factors influencing health'. Leukaemia cases had the highest number of admissions compared with other diagnostic groups.

The ranking of cause of admission from the highest percentage to lowest were similar during the on treatment and post-treatment phases, however, some causes had lower percentages of admissions after completion of cancer treatment, such as admissions for 'neoplasm' causes, which decreased from 83% to 47% of total admissions during the on treatment and post-treatment phases, respectively. While the remaining percentage of cause of admission was slightly higher during the post-treatment phase than on treatment period.

The percentages of admissions for 'certain infectious and parasitic diseases', 'diseases of the blood', 'symptoms, signs and abnormal clinical and laboratory findings', 'injury, poisoning and certain other consequences of external causes' and 'factors influencing health status' were higher during the on treatment phase than post-treatment phase for the majority of diagnostic groups, except for germ cell tumours. Similarly, the rate of admissions for 'respiratory diseases' was higher during the on treatment phase, except for lymphoma, CNS, renal tumours and germ cell tumours.

Three-quarters of the cancer survivors were readmitted to hospital after completion of cancer treatment and those were mainly for causes coded as 'factors influencing health'. Within which, children were admitter significantly earlier than TYAs for the majority of causes (median overall was 0.17 and 1.17 respectively, *P*-value=<0.001), except for admissions due to 'mental and behavioural disorders' and 'diseases of the eye', not significantly though. Leukaemia and bone tumour survivors had the earliest admissions after completion of cancer treatment.

After completion of cancer treatment, about a third of the cases were admitted for neoplasm proposes (disease of the recurrent malignancy or subsequent primaries combined), in which the median time to first admission for those cases for all cancers combined was within one year of treatment completion, and it was shorter for children than TYAs, and was significantly shorter for leukaemia, lymphoma and CNS tumours.

The cancer cohort had about three times the number of admissions than the background population, and mainly for ‘diseases of the blood’ and ‘neoplasms’.

Leukaemia, bone tumour and CNS tumour survivors had the highest SHR compared with other diagnostic groups. While, germ cell tumour survivors had the lowest standardised incidence rate. Leukaemia and bone tumour survivors had the highest SHR for ‘endocrine, nutritional and metabolic diseases’ and ‘diseases of the circulatory system’ apart from neoplasms. While among CNS survivors, the SHR was highest among ‘diseases of the nervous system’ just after neoplasm-related admissions.

The SHR was higher among children than TYAs, apart from endocrine-related causes. The three highest causes of admission among children were ‘neoplasms’, ‘diseases of the blood’ and ‘circulatory diseases’, while among TYAs were for ‘diseases of the blood’, ‘neoplasms’ and’ endocrine diseases’. The rate of pregnancy was lower among cancer survivors than the background population, and was lower among children than TYAs.

For all causes combined, males had a higher SHR than females, however looking at detailed causes of admission, males had higher rates of admission only for ‘neoplasms’, ‘diseases of the blood’ and ‘diseases of the nervous system’.

Chapter 9 Discussion

9.1 Introduction

This study primarily aimed to investigate patterns of hospital admissions among children and young people (CYP) with cancer following their diagnosis and during their treatment. It also aimed to identify hospital-related comorbidities upon treatment completion using a high-quality, specialist population-based cancer register and linked hospital activity data.

Healthcare commissioners in England set an aim to improve the quality of life for cancer survivors, a population which is expected to grow to over three million people in England by 2030, by enhancing planning for services to meet their needs [16]. In order to plan for services, it is vital to understand the healthcare utilisation of cancer survivors and their related comorbidities. Therefore, this thesis, for the first time, provides a comprehensive analysis of cancer care, healthcare burden and related morbidity among cancer survivors from date of diagnosis and beyond for children and young people. The focus on morbidity that leads to hospitalisation emerged during the 20th century, and to date, research had mainly concentrated on long-term survivors, who were cancer free for more than five years following diagnosis [15, 23, 87, 92, 101, 140, 147, 149, 150]. However, little attention had been paid to the shorter term healthcare burden among survivors of CYP cancers [24].

Therefore, this thesis addresses a key knowledge gap by analysing the healthcare burden for all hospital-related causes among cancer cases during the treatment period following cancer diagnosis, as well as the period following treatment completion within and beyond five years from diagnosis. The purpose was to understand the risk of future hospitalisation and the size of the hospital burden on NHS services, so these can be planned locally and regionally in Yorkshire, given the unique population and ethnic diversity. The burden from hospital admissions during and after cancer treatment varied by cancer type, age group, gender, ethnicity, deprivation, and according to the proportion of time in specialist care services. The key novel findings which have arisen from this thesis are summarised below. These representing observational finding, and could be used as benchmark for future study to identify the reasons behind increasing the hospital burden among the below specified groups.

Finding 1: Bone tumour and leukaemia survivors had the highest risk of hospital admissions, and stayed longer in hospital during the treatment period and after treatment completion.

Finding 2: TYAs aged 15-29 years at diagnosis had significantly (2%) lower levels of hospitalisation than children aged 0-14 years for all cancers combined, and for the majority of cancer types, except for leukaemia and renal tumours. Children received the vast majority of their care in specialist settings, and had a higher amount of specialist care compared with TYAs. Furthermore, children were more likely to return to hospital after completing their treatment, earlier and more often than TYAs.

Finding 3: Females had higher levels of hospital activity in terms of length of stay compared with males, except for cases diagnosed with CNS tumours, where the opposite effect was found. Although the incidence rates of cancer were higher among males than females in the 0-29 years age range, especially for lymphoma and germ cell tumours, females with lymphoma and germ cell tumours had a higher median rate of admissions than males. Both males and females had a higher rate of admission than the background population, and males had a higher excess rate of admissions after treatment completion compared to females, especially those classified as for 'neoplasms', 'diseases of the blood' and 'diseases of the nervous system'.

Finding 4: Although South Asians had higher rates of admission compared with non-South Asians for all cancers combined, this difference was not significant after adjusting for patient case mix, except for STS where South Asians had 42% lower admission rates than non-south Asians. A relationship between ethnicity and disease severity was found in previous studies, such that Asians with leukaemia, CNS or germ cell tumours were likely to have a poor prognosis, which may explain the higher rate of admissions observed in this thesis [49].

Finding 5: Socioeconomic status did not have a significant effect on the frequency of hospital admissions apart from those diagnosed with CNS tumours: cases from the least affluent areas were more likely to be admitted to hospital and stayed longer than cases from the most affluent areas, an effect which remained after adjusting for disease severity.

Finding 6: The common causes of post-treatment admissions among cancer survivors varied by cancer type, age group and gender. Such admissions were mainly attributed to 'neoplasms' and 'diseases of the blood'.

Finding 7: Cancer survivors were at a higher risk of hospitalisation than the background population for various reasons after treatment completion.

A detailed discussion of the main findings is presented in the following sections by comparing the results with the available literature. The burden of hospital activity and related morbidity after diagnosis with cancer was analysed in two distinct phases, and results relating to each phase are discussed in the following sections: 1) on treatment period (Section 9.2), and 2) post-treatment period (Section 9.3). Within each section, the main findings are discussed relating to the hospital burden (the number of admissions and length of stay) and the cancer-related morbidities (focusing on the causes of admission).

The factors that influenced hospital activity during the complete follow-up period are summarised separately by cancer types and for all cancers combined in Section 9.4.

Finally, the clinical implications of the work are discussed in Section 9.5, the strengths and limitations of the work in Section 9.6 and 9.7, recommendations for future work in Section 9.8 and an overall conclusion is provided in Section 9.9.

9.2 Hospital admissions during the treatment period

This thesis comprises the first health services research study to analyse the in-hospital burden of healthcare utilisation during the treatment period for CYP diagnosed with cancer. Importantly, the analysis accounted for variations in treatment duration when assessing rates of hospitalisation. Furthermore, the cause of admission during the treatment period was studied in detail to help understand the scope of services needed, according to cancer type and age group.

During the treatment period, there were 2,645 individuals with 49,831 admissions, with a median of 12 admissions per person (median of one follow-up-year per person, IQR 1-2 years). In addition, cancer patients were in hospital for a total of 180,385 bed days during their treatment period, with a median of eight bed days per 100 person-days.

Overall, children had a higher median number of admissions than TYAs for all cancers combined, having 16 and 9 admissions per person per year, respectively. In addition, children also had longer hospital stays during the treatment period than TYAs in all cancer types, except for leukaemia survivors (median length of stay = 11 and 27 days per 100 person-days for children and TYAs, respectively).

Leukaemia survivors had the shortest time interval from diagnosis to first treatment with a median of one day among children and seven days among TYAs; 85% of leukaemia survivors were initially treated with chemotherapy. This, therefore, may have partly explained the highest pattern of admissions seen among leukaemia survivors compared with all other TYA survivors and the second highest admission rates among children. Patients receiving chemotherapy require frequent visits to hospital to receive their

treatment. Therefore, patients receiving chemotherapy are expected to have a higher number of admissions.

Bone tumours had the highest median number of admissions among children and the second highest among TYAs, having 21 and 14 admissions per person per year, respectively. Additionally, CYP diagnosed with bone tumours had the longest hospital stays of 20 days on per 100 person-days during the treatment period compared with all other cancer types, where the median length of stay ranged from 4 to 17 days per 100 person-days.

During the treatment period, the most common causes of admissions were for treatment-related conditions, including ‘certain infectious diseases’, ‘neoplasms’, ‘diseases of the blood’ and ‘respiratory diseases’, which varied by cancer type. Most cancers saw hospital admissions with such causes during the treatment period, however some other causes also commonly occurred both during the treatment period and after treatment completion for certain cancer types. These were: ‘diseases of the nervous system’ among leukaemia, bone tumour and germ cell tumour cases; ‘diseases of the digestive system’ among leukaemia, neuroblastoma, bone tumour and STS cases; ‘disease of the circulatory system’ among CNS and neuroblastoma cases; ‘diseases of the skin’ among leukaemia, CNS and neuroblastoma cases; and ‘diseases of the musculoskeletal system’ among leukaemia and bone tumour cases. The cause and the pattern of hospital usage before treatment completion had not been studied up to now. Therefore, this novel finding could highlight the complications that short-term survivors may experience and, therefore, the appropriate services that need to be available to manage these complications and meet the needs of young people.

9.3 Hospital admissions during the post-treatment period

One of the unique features of this work is the ability to help understand the hospital burden among cancer survivors from the point of treatment completion. Findings provide new knowledge on the frequency of admissions and length of stay in hospital, as well as the related causes of admissions, in order to plan for services immediately after completing cancer treatment and in the subsequent follow-up period.

There were 2,304 cases who survived after treatment completion, 1,723 (75%) of which were admitted at least once after treatment completion and contributed to 12,140 admissions with a median of three admissions per survivor. Additionally, they were hospitalised for 34,943 person-days with a median of six bed days per 100 person-days.

Following treatment completion for all cancers combined, children had higher median rates of admission than TYAs, having 0.64 and 0.39 admissions per person-year,

respectively. However, TYA leukaemia and renal tumour survivors had a higher median number of admissions per person-year than children after treatment completion (Figure 33). In terms of the number of days spent in hospital, children had longer hospital stays after completion of cancer treatment than TYAs, except for neuroblastoma and renal tumour cases, although TYA numbers were very small for these two latter groups.

Children and young people with leukaemia and bone tumours had the highest hospital admission rates after treatment completion with 0.8 and 1.6 admissions per person-year on average. Additionally, CYP with bone tumours had the longest hospital stays out of all cancer types, with a median duration of 0.41 days per 100 person-days after completion of cancer treatment.

Based on the results from the literature review in Chapter 3, only one study assessed the cancer-related effect during treatment phase, and focused on one specific cancer type (leukaemia and CNS tumours) [79]. Causes of morbidity considered as being long-term cancer-related effects, such as ‘diseases of the circulatory system’, ‘mental disorders’, and ‘endocrine disorders’ [25, 49, 72, 87], were consistent with the thesis findings, as survivors were commonly admitted for these causes after they completed their treatment. Additionally, and contrary to other cancer types, ‘diseases of the respiratory system’ admissions occurred more often after treatment completion among lymphoma, CNS and renal tumour cases than during the treatment period. This suggests that different healthcare services need to be available at different stages of the life course for these cancer types.

Using age, sex and attained year matched background population data, the excess rates of hospital admissions after treatment completion were analysed for all causes combined and separately by main causes of admissions. Cancer survivors were at a significantly higher risk of admission than the background population (SHR=2.37, 95% CI:2.26-2.49), except for pregnancy. This was a similar finding throughout the literature focused on long-term survivors, whereby the risk of admissions compared to a comparison or control group varied between 1.4 and 5.1 [12, 15, 23, 70, 71, 101, 149]. However, these studied focused on one age group, either childhood survivors (aged 0-20 years) [12], young people survivors (aged 20-24 years) [23], or on specific cancer types (HL) [70], or specific morbidity (cardiovascular diseases) [71]. Common causes that showed the highest frequency of admissions after completion of cancer treatment were ‘neoplasms’, ‘diseases of the blood’ and ‘other factors influencing health’.

The rate of pregnancy was lower among the cancer cohort compared with the background population (SHR=0.9, 95% CI: 0.7-1.2), probably explained by the higher prevalence of infertility within the cancer cohort, especially among TYAs due to the type of treatment received and the associated toxicity. When assessing the frequency of

admission for pregnancy causes by age at diagnosis, TYAs had a higher rate of admissions compared with children, adjusting for rates of admissions among the background population. This could reflect the fact that TYA survivors might suffer from infertility and delays in pregnancy more than childhood survivors, for example, some studies found that females aged 13-20 years suffered from ovarian failure more than females aged less than 13 years old [204].

Childhood survivors were admitted earlier after treatment completion than TYA survivors for all causes combined (median=0.17 and 1.17 years, respectively). Additionally, children had a higher risk of excess hospitalisation than TYAs. This could be related to the fact that children were either more sensitive to the effects of chemotherapy or radiation therapy, or they had an excess risk of developing treatment-related complications, such as obesity, endocrine disorders and cardiomyopathy, in relation to the type of treatment received [14, 154, 205].

For all causes combined, males had a higher excess rate of admissions than females, having 2.8 and 2.0 times higher chance of hospitalisation, respectively, compared to the background population. However, the causes of these admissions were mainly for ‘neoplasms’, ’diseases of the blood’,’ diseases of the nervous system’ and ‘factors influencing health status’. The hospital admissions among 20,275 five-year survivors between 1992 and 1999 in Ontario, Canada, was studied and it was found a slightly higher relative rate of admissions among males than females of 1.7 and 1.5 respectively, compared with the background population [149]. Similarly, in another study of 1,564 five-year survivors in 1996 to 1999 in Amsterdam, Netherlands, males displayed higher relative rates of admissions than females compared with the background of 2.4 and 2.0 times higher, respectively [150]. Based on these findings, it can be assumed that males are more likely to suffer from cancer-related diseases resulting in hospitalisation almost immediately after completing cancer treatment, compared to females.

Bone tumour and leukaemia cases had the earliest readmissions to hospital after completing cancer treatment out of all types. Furthermore, leukaemia survivors had the highest excess rate of admission followed by renal tumours, bone tumours and CNS tumours for all causes combined, when compared with the background population. Similarly, in previous studies it was found that the hospitalisation rate among young people with leukaemia exhibited the highest relative rate of admission compared with the matched control group as found in previous studies [148]. Their study focused on morbidity among long-term survivors of cancer aged 20-24 years at diagnosis. They found that the common causes of admissions were for blood diseases, excluding admissions for recurrent neoplasm, this was similar to this thesis finding, as admissions for blood disorders were responsible for the second highest number of admissions after

neoplasms. Neoplasms had the highest excess rate of admissions among young people survivors in the study conducted in British Columbia, Canada comprising 902 survivors [23], which supports the finding of this thesis. One other long-term cancer survivor study found that CNS survivors had the highest excess rate of admissions compared with the background population [150], possibly due to the time frame that was used to estimate the health burden. In this study, they only considered five-year and beyond survivors from the date of diagnosis, whilst in this thesis, health burden was calculated from the date of treatment completion and that could be one year after diagnosis, i.e. it considered admissions occurring before five survival years after diagnosis.

The most common form of morbidity that lead to hospitalisation varied by cancer types. Leukaemia had the highest excess rate of admissions due to the following causes, 'certain infectious diseases', 'diseases of the blood', 'diseases of the respiratory disease', 'symptoms and signs of abnormal clinical findings', 'injury, poisoning and other external causes', and 'factors influencing health'. CNS tumours had the highest excess rate of admissions for the following causes: 'endocrine, nutritional and metabolic disease', 'diseases of the nervous system', and 'diseases of the eye'. Neuroblastoma survivors had the highest excess hospitalisation rate for 'mental and behavioural disorders', and 'diseases of the musculoskeletal system'. Renal tumour survivors had the highest excess risk of admissions for 'diseases of the circulatory system' and 'congenital malformation' compared with all other cancer types.

9.4 Hospital admissions during the complete follow-up period

The study comprised a total of 3,184 tumours pertaining to 3,151 individuals who contributed 22,104 person-years in the period from 1996 to 2009 in the former region of Yorkshire, with at least one post-diagnosis inpatient hospital admission. These individuals were responsible for 65,925 inpatient hospital episodes between January 1997 and December 2011, with a median of 6.3 admissions per person per year. The total outpatient admissions were 114,496 hospital visits, with a median of 39 and 19 visits per person for children and TYAs, respectively. Additionally, the cancer cohort remained in the hospital as an inpatient and stayed for 215,328 person-days with a median of one day following diagnosis with cancer per 100 person-days.

The factors that could affect the likelihood of hospital admission and length of stay following the point of diagnosis were analysed using descriptive and multivariable analysis. The univariable analysis was the focus of Chapter 6 and included a detailed analysis of the median number of admissions, adjusting for person-years of follow-up according to various explanatory variables, such as age at diagnosis, gender, ethnicity, deprivation and relapse status. The multivariable analysis used to estimate the rate ratio

of admissions and duration of inpatient admissions adjusting for patient demographics and clinical characteristics using negative binomial regression formed the basis of Chapter 7. These characteristics were: age at diagnosis, gender, ethnicity, deprivation, year of diagnosis, relapse status, proportion of specialist admissions/stays, and type of initial treatment. Their impact on admissions and length of stay varied by cancer type, therefore each main cancer typed is discussed separately in the following sections. The study focused on eight main cancer groups which accounted for the majority of cancers occurring among 0-29 year olds: leukaemia, lymphoma, CNS, neuroblastoma, renal tumours, bone tumours, STS, and germ cell tumours. Further justification for choosing these cancer types is mentioned in Chapter 4, Section 4.5.

9.4.1 Leukaemia

In univariable and multivariable analysis the age had an effect on the length of stay, TYAs had more than double the lengths of stay compared to children post diagnosis. This could be due to the fact that TYAs are more likely to be diagnosed with AML more often than ALL, in contrast to children where ALL is more common. As explained in Section 2.3.6, AML has a much poorer prognosis than ALL.

After adjusting for demographic and clinical factors (age, sex, year of diagnosis, ethnicity , deprivation, proportion of specialist care, relapsed status and type of initial treatment), year of diagnosis, relapse status and type of initial treatment were all significant predictors of hospital admissions among leukaemia cases. Relapse cases represent higher risk cases than those who did not relapse, and are usually treated with intensive treatment, such as a bone marrow transplantation. Approximately 15% of leukaemia survivors received a BMT, of whom 47% relapse at least once. Survivors having a BMT may suffer from a weak immune system, and consequently be admitted to hospital due to infectious diseases, bleeding and liver disease [206].

Cases treated with chemotherapy and radiotherapy, or with chemotherapy and surgery had significantly higher hospitalisation rates than cases treated with chemotherapy alone, after accounting for person follow-up years, patient demographic factors, relapse status and the level of specialist care. This finding was similar to what has been found previously, in that survivors treated with chemotherapy and surgery required a higher level of day care during treatment compared with survivors who had received other treatment modalities, with double the hospitalisation rate compared to cases with another treatment modality [140]. On the other hand, results showed that survivors treated with radiotherapy alone were found to have significantly lower admission rates than survivors treated with chemotherapy alone. In contrast, other studies found that survivors treated with radiotherapy had higher hospital admissions than survivors treated with surgery alone [140]. However, in their analysis the effect of treatment on hospitalisation was

limited to long-term survivors and their analyses were not separated by cancer type. Additionally, they used surgery alone as a reference group in their statistical modelling, instead of chemotherapy, and their finding was not significant. In this thesis, leukaemia survivors treated with chemotherapy alone were the most common treatment modality grouping and, therefore, chosen as the reference group to ensure robust parameter estimates. As explained in Chapter 2, leukaemia survivors were expected to have concurrent admissions during their treatment period to receive chemotherapy in different cycles or regimes at different time points for around six cycles that could last up to 10 months for ALL tumours, compared with one cycle of radiotherapy [29]. In comparison to leukaemia cases who were initially treated with chemotherapy alone, survivors treated with radiotherapy had shorter hospital stays. This could be explained by the limited number of survivors treated with radiotherapy in this study compared with survivors treated with chemotherapy. Additionally, the chemotherapy regime included multiple treatment cycles during the remission stage, and it was found that survivors of AML on average stayed for around 30 days per cycle [206]. Chemotherapy is usually administered as a day care surgery procedure or an outpatient admission [79, 140], while surgical procedures require longer inpatient stays to monitor patients' health before and after surgery.

9.4.2 Lymphoma

Lymphoma cases contributed to 22% of all admissions from the Yorkshire registry cohort with a median of 16 inpatient admissions per person. This was the most common cancer type among TYAs. A study, conducted in the USA, assessed the prevalence of admissions among long-term survivors of childhood and young adult cancer aged 0-20 years and found that the risk of hospitalisation was highest among lymphoma, rather than leukaemia survivors [12]. However, their analysis was based on questionnaires rather than (electronic) hospital records, therefore may have been prone to typographical and other recording errors during the transcription process. It also highlights the level of morbidity that might exist among these survivors, emphasising the importance in understanding the hospital burden and, accordingly, planning of appropriate services.

Age at diagnosis, gender, deprivation, ethnicity and proportion of time spent within specialist hospital providers had no impact on the patterns of hospital admissions for this cancer group. However, the type of initial treatment had a significant effect on the rate of admission after adjusting for demographic and clinical factors. Survivors who received chemotherapy had the highest admission rates compared with any other treatment modality. This was similar to leukaemia survivors, suggesting that the management of chemotherapy included more frequent visits to hospital to receive treatment and to recover from certain side effects of treatment, compared to other treatment modalities.

Lymphoma survivors were one of the cancer types that received relatively limited levels of admissions to specialist centres. However, length of stay was longer among survivors receiving more of their care from specialist units during the off-treatment and follow-up period. This could suggest that lymphoma survivors who received most of their care in specialist units had longer stays in hospital after diagnosis of their cancer than those who were primarily seen in non-specialist units. This could be due to the stage or severity of disease among cases treated in specialist units, as there is evidence that patients treated in principal treatment centres had a poor prognosis compared to those seen in non-PTC units [127]. However, in the current analysis disease severity was adjusted for using type of initial treatment and relapse status. Survivors with a poor prognosis often experienced relapses of the disease and were treated on more aggressive regimes than other tumours with a better prognosis. In the current analysis these factors were taken into account, drawing the conclusion that there is a clear relationship between level of specialist care and length of stay.

9.4.3 CNS tumours

Children diagnosed with CNS tumours had significantly higher rates of admission than TYAs, indicating that either children needed to be treated quite often in an inpatient setting compared to TYAs, or that they were more susceptible to treatment side effects than TYAs.

Female CNS tumour survivors had significantly shorter hospital stays than males in the multivariable analysis. This was a novel finding as there have been no previously published studies which compared cancer-specific hospital activity by gender or other patient characteristics.

The other significant predictor of hospitalisation was deprivation, such that those diagnosed in the most deprived areas had more hospital admissions than those from the least deprived areas after adjusting for relapse status, disease severity and place of care. The percentage of CNS tumour cases in Yorkshire was found to be varied by place of care and management of treatment over the study period (1990-2009) [127]. Year of diagnosis was adjusted for in the current analysis to reduce the effect of confounding data due to changes in healthcare delivery over time, with results showing that the number of admissions increased by 4% (95%CI:2-7%) throughout the study period.

CNS tumour patients from the most deprived areas at diagnosis had higher admission rates compared to those from the least deprived areas. There have been no published studies to analyse the pattern of healthcare activity among CNS tumours specifically in relation to socioeconomic status. However, a study from Taiwan included 32,800 cancer deaths and found that cases associated with low socioeconomic status were more likely

to receive more aggressive care in terms of hospitalisation and type of treatment received than cases with high socioeconomic status during the end of their life [207]. Although not specific to CNS survivors, long-term admissions for 'respiratory diseases' and 'other external causes of morbidity' significantly increased with levels of deprivation [101]. Although to date no reasonable explanation has been presented for this fact, it could be understood that cases with low socioeconomic status might be presented with more aggressive/advanced cancer types.

Surgery alone was the most common form of treatment for CNS survivors within the study population, whereby these cases had lower admission rates than those who were treated initially with chemotherapy alone. Similar to leukaemia survivors, this could have occurred due to the nature of chemotherapy, which requires a longer hospital stay than surgery alone, and may also require monitoring for longer periods in case of any subsequent treatment-related admissions, as compared to surgery alone.

The amount of time seen within specialist care services also had a significant effect on length of hospital stay, so that those receiving mostly specialist care services had a shorter hospital stay than those who had limited or no specialist care. Those who received their care based within high-volume oncology departments had shorter hospital stays on average compared to those who did not [22].

9.4.4 Neuroblastoma

Due to the limited number of diagnoses within this group, it was not possible to identify significant factors associated with the likelihood of admissions and hospital duration. This could be the focus of a future study by including more cases derived from either national or international datasets to identify the predictors of hospital activity for survivors of neuroblastoma.

9.4.5 Renal tumours

Contrary to what was observed for CNS survivors, TYAs diagnosed with renal tumours had higher rates of admissions compared with children based on results from the multivariable analysis. Renal tumour patients received mostly specialist care, and had significantly higher rates of admissions and longer hospital stays compared to those who received only limited specialist care.

9.4.6 Bone tumours

In addition to the year of diagnosis and relapse status (where the number of admissions and lengths of stay increased for more recent years of diagnosis and for those who relapsed), children had higher rates of admission than TYAs. This finding is supported by earlier work explained in the literature review in Chapter 3, that children are sensitive to the treatment side-effects for radiotherapy and chemotherapy, such as a higher risk

of cardiac complications due to chemotherapy agents, and other mental diseases as a result of radiation exposure [12, 14, 33, 154].

9.4.7 Soft tissue sarcoma

STS was the only cancer type that showed an association between ethnic group and admission rate and length of hospital stay. South Asians had lower rates of admissions and lengths of stay than non-South Asians. The only other vaguely similar study from the literature which supported this finding was from a study conducted in Spain, which found that foreign citizens who came from high or low economic countries had lower rates of admissions than local citizens [208]. However, two key limitations of the study was that the analyses related only to adult admissions and they did not specifically refer to cancer survivors.

9.4.8 Germ cell tumours

Children aged 0-4 at diagnosis had higher rates of admission than older children and TYAs. Additionally, older children had shorter hospital stays than younger children. Survivors who received most of their admissions in specialist care settings had fewer hospital admissions and a shorter length of stay than survivors who receive limited specialist care admissions.

9.4.9 Overall cancers combined

9.4.9.1 Cancer types

Leukaemia diagnoses accounted for 40% (24,502 admissions) of total post diagnosis inpatient admissions and 36% (40,959 admissions) of outpatient admissions. Survivors treated with both chemotherapy and surgery were found to be at a higher risk of an inpatient admission compared to any other treatment modality [140]. This supports the fact that higher admission rates were seen among leukaemia cases compared with other cancer types, since 88% of these individuals received chemotherapy and surgery as part of their main treatment. Among those cases, inpatient admissions and outpatient admissions were higher among children than TYAs, with a median of 41 and 20 inpatient admissions, respectively, and 80 and 21 outpatient admissions, respectively (Chapter 6, Figure 33 and Table 35). Children had a pronounced difference in inpatient admission patterns compared with outpatient admissions, while the difference was much less marked among TYAs. This was supported by findings from other studies who showed that leukaemia survivors experienced more outpatient admissions than inpatient admissions [79]. This could be explained by the type of treatment received, as childhood leukaemia patients commonly receive their chemotherapy in an outpatient setting [160]. There are several reasons which could explain the difference in inpatient and outpatient admissions between children and TYAs: one reason could be because of compliance to

treatment, whereby TYAs could be less compliant with their treatment regime [209], thereby also affecting compliance with outpatient admissions. Another reason might be the difference in leukaemia histological subgroups: ALL is a more common subtype among children while AML is common among TYAs, resulting in different treatment management. Furthermore, the cytogenetic characteristics of leukaemia are different among children compared to adolescents and young adults, with more favourable cytogenetic profiles commonly seen in children compared to TYAs [210]. Additionally, in contrast to children, TYAs are less likely to receive most of their care in a specialist unit given the variation in place of care for this age group, possibly leading to different outcomes [134]. For example, in this study, only 42% of TYAs received the majority of their admissions in specialist centres, compared with 85% of children (Chapter 5, Section 5.3.3.5).

Although bone tumour survivors accounted for only 7% of total admissions, they were responsible for the highest median number of admissions among children, and the second highest number of admissions among TYAs. This was similar to what has been reported in a study conducted among long-term childhood and adolescent survivors, where bone tumours had the highest ratio of admissions adjusting for the background population than other cancer types [15]. In their paper, Kirchhoff, et al. argued that bone tumour survivors may suffer from severe long-term side-effects of treatment, such as cardiomyopathy and other physical complications that explain the elevated risk of admission [15]. Furthermore, bone tumour patients may experience higher rates of admissions for second malignancies compared with leukaemia, as reported in a study which focused on childhood bone tumour survivors [24]. Results from this thesis support these findings, such that bone tumour survivors had the highest rate of relapse with around 25% of cases experiencing recurrent disease in the current analysis.

9.4.9.2 Age group at diagnosis

Children had a higher median number of admissions adjusted for person-years of follow-up than TYAs, with an average of four and two admissions, respectively, per person. This was consistent with the literature [12], with children more likely to require higher levels of hospital admissions due to the complexity of the disease. Additionally, the increased risk of hospitalisation among children may also be related to the fact that they are still growing, and their organs may be more sensitive to the type of treatment received, therefore more likely to develop long-term effects on organ development [12]. Additionally, the nature of the treatment could elevate the frequency of admissions and length of stay for the younger age group, where their treatment is usually more intensive than TYAs [101].

9.4.9.3 Ethnicity

South Asians had a higher median number of admissions than non-South Asians for all cancer types, except for STS. However, the multivariable analysis results showed that the effect of ethnicity was only significant among STS. The limited number of cases and, therefore, power could have led to a failure to identify the influence of ethnicity on hospital activity for other cancer types. Nevertheless, this finding warrants further investigation in larger populations according to ethnic group, to confirm whether this effect can be replicated.

9.4.9.4 Deprivation

The rate of admissions was significantly higher among those from the most deprived areas, compared to those originating from the least deprived areas. In a Canadian study that investigated hospital activity and socioeconomic disparities, income was used as a proxy for deprivation [211]. Similar results were seen, such that those with lower incomes tended to have higher hospital admissions than those with higher incomes, suggesting that individuals from lower income households require more hospital care, even after a cure from their cancer.

9.4.9.5 Year of diagnosis

For all cancers combined and for all cancer subtypes, the rate of admission and length of stay significantly increased by year of diagnosis. This finding could be explained by improvements in the recording of admissions within HES data over time. The payment by results system was introduced in 2002/2003. It was issued as a tool to monitor health service quality among NHS settings, and consequently, as a mechanism through which NHS trusts received their annual funding. The rate of admissions based on year of diagnosis increased from 3% in 1997 to 7% in 2009 (Figure 29), with a slight increase in admissions after 2003; 48% of total admissions occurred before 2003 and 52% after 2003. The results from the multivariable modelling (adjusting for person-years) showed that after separating cases into those diagnosed before and after 2003, the rate of admission increased significantly by 53% per person (95% CI: 41-66%) among cases diagnosed after introducing payment by results. This artefactual increase in recording of HES records needs to be borne in mind when interpreting findings from this thesis.

9.4.9.6 Gender

Differences in the median number of inpatient admissions by gender were fairly modest with a slight excess among females compared to males (medians of 2.5 and 2 per person per year for females and males, respectively). This was consistent with some of the previous studies , that reported a similar rate of admission between males and females [149]. Another study, conducted in the USA, found a slight increase in the incidence of admissions among females compared to males, with incidence rates of 108.5 and 177.3

admissions per 1,000 person-years for males and females, respectively. Both of these studies refer to five-year cancer survivors, therefore information on admissions during treatment or immediately after treatment completion was not included. As yet, there have been no reported studies to analyse hospital activity beyond the date of diagnosis, thus precluding any formal comparisons with the current work reported in this thesis. Thus, the results of this current work provide the first detailed health services research study on hospital use from the date of diagnosis and beyond.

9.4.9.7 Year of admission

During the admission study period from 1997 to 2011, the percentage of admissions by year of admission increased from 4% in 1998 to 6% in 2010 (Chapter 6). This percentage fluctuated during the study period and peaked during 2005 to 2007 with 9% of total admissions, reflecting the increase in cancer incidence rates observed in 2005, when rates also peaked at 205 per million person-years.

After adjusting for person-years, the median number of admissions and length of stay decreased over time for the majority of main cancer types (Chapter 6, Figure 49 and Figure 53). This was supported by findings in Canada, where the rate of hospital admissions also decreased over time [149]. However, their analysis was limited to survivors of young adult cancer aged 20-44 years at diagnosis, and who survived more than five years from diagnosis.

However, the pattern of admissions among childhood bone tumour patients began to increase more than eight years after treatment completion. This could raise future clinical concerns for long-term bone tumour survivors, so that appropriate services can be planned and made available.

9.4.9.8 Level of specialist care

The National Institute for Health and Care Excellence (NICE) set out guidelines to trusts in England, in order to provide optimal cancer care and outcomes for children and young people [11]. The guidelines included recommendations for specific age-appropriate cancer services, as described in Section 2.4.

Cases were classified as receiving specialist care if they were admitted to a PTC or cancer specialist centre (more detail in Chapter 4). For all cancers combined, around 45% of survivors received most of their admissions in specialist units (Chapter 5, Figure 21). Children aged 0-14 years had a higher percentage of admissions in specialist units compared to TYAs aged 15-29 years. This could be explained by the lack of consistency in cancer referrals to specialist units for TYAs. Although the majority of children and TYAs in the current study received their care in specialist centres, mainly Leeds General Infirmary and St James's University Hospital, other specialist centres where patients

were managed included Sheffield Children's Hospital and Birmingham Children's Hospital (Chapter 4, Section 4.11.6).

The median number of admissions was higher among those who had the majority of their admissions in specialist cancer units (median=21, IQR=8-40). The difference in the median number of admissions was more pronounced during the treatment period for those seen mostly in specialist units, receiving a median of 18 admissions during the treatment period, compared with seven admissions among those seen much less often in specialist services. The difference in admissions was more modest after treatment completion, with median numbers of four and three admissions, respectively. This could suggest that cases referred to specialist centres might be cases with more advanced disease or may be being treat with more complex modalities.

The impact of level of specialist care units on hospital admissions and length of stay was similar before and after adjusting for age, sex, ethnicity, deprivation and type of initial treatment: cases receiving a higher proportion of specialist care had an increased number of hospital admissions and a longer stay in hospital. This varied by cancer type, as explained previously in Sections 9.4.1 to 9.4.8.

9.4.9.9 Initial treatment

Cases initially treated with chemotherapy and radiotherapy in combination had higher rates of admission and stayed longer in hospital than cases treated with chemotherapy alone. In contrary, other type of initial treatment such as surgery alone, radiotherapy alone, or combination of both had lower ate of admissions and stay for shorter period than cases treated with chemotherapy alone. This could indicate that those who received chemotherapy visited hospital more often to receive treatment, or perhaps could be due to complications of the treatment [12]. It was found that out of all long-term survivors, those treated with chemotherapy had the highest hospitalisation rate, ranging from 135.9 to 185.3 per 1,000 person-years dependent on the chemotherapy agents used (Anthracyline, Bleomycin and Cisplatinum) in previous studies[12]. However, in their study only radiation therapy was significantly associated with an increase in hospitalisation rates compared with the background population, after adjusting for demographic characteristics. Similarly, some studies found an increase in the number of admissions among long-term survivors treated with radiotherapy [70, 140, 150]. This finding does not necessarily contradict those within this thesis, as the data structure and analysis was different, focusing on the effect of treatment on both short- and long-term survivors after being diagnosed with cancer. Therefore, the increase in hospitalisation among cases treated with chemotherapy compared with other treatment modalities could have arisen due to consideration of the period before completion of cancer treatment.

In this thesis, several data sources were used to identify the type of initial treatment, notably a specialist population-based cancer register, HES and direct abstractions from medical records. The recording of treatment in the cancer register was significantly better than HES, as around 91% and 97% of total cases were recorded as receiving chemotherapy and radiotherapy, respectively, compared to only 75% and 5% from within HES. Furthermore, there were still 9% of cases who had no reported treatment despite cross-checks from multiple sources, as listed above.

It was found that cases with no record of any initial treatment had significant lower rates of admission than cases treated with chemotherapy alone when diagnosed with lymphoma, CNS, neuroblastoma, bone tumours, STS and gem cell tumours. Additionally, these individuals had a significantly shorter hospital stay compared with those treated with chemotherapy alone among CNS, bone tumours and germ cell tumours. Cases with CNS tumours had the highest percentage of cases with no recorded initial treatment, possibly explained by the fact that this group would include certain benign tumours, necessitating patients being monitored for any tumour progression.

9.4.9.10 Relapsed disease

This study identified the pattern of admissions among relapsed cases, in contrast to those who did not experience a relapse of their disease, from the date of primary diagnosis to date of relapse. The purpose was to provide information on hospital burden from relapse for healthcare planners. The majority of relapsed cases were diagnosed with bone tumours. The median time to relapse varied by diagnostic group: for all cancers combined this was 17 months after diagnosis, and ranged from 8-20 months according to cancer subtype. For diagnostic groups such as leukaemia, where the median time to relapse was 20 months from diagnosis, the pattern of admissions overall was higher among relapsed cases than those who never relapsed, evident even from the date of diagnosis. The difference in the median number of admissions for those who relapsed compared to non-relapsed cases was significant 48 months after diagnosis.

The difference in the pattern of admissions over time among relapsed and non-relapsed cases was pronounced in terms of length of stay, since relapsed survivors had significantly longer hospital stays compared to non-relapsed survivors, especially among cases with lymphoma. However, this difference was less pronounced among leukaemia, CNS and bone tumour cases.

Cases who relapsed had significantly higher rates of admission and stayed longer in hospital than those who did not relapse. Excluding relapsed cases from the analysis did not affect the factors that impacted the rate of hospitalisation, for example the rate of admissions decreased by each single year increase in age.

The predictors of admissions among relapsed and non-relapsed cases were similar, except for the proportion of specialist care. Relapsed cases had shorter hospital stays among cases receiving totally specialist care, compared to cases receiving non-specialist care, while the opposite pattern occurred among non-relapsed cases. This could suggest that survivors with poor disease prognosis at diagnosis were more likely to receive their care in non-specialist units, while non-relapsed survivors, who may be more likely to have less advanced disease at diagnosis receive the majority of their care in specialist cancer settings. Moreover, those with a very poor prognosis may have been transferred to a hospice or other palliative care service to deal with terminal illness. PTCs or specialist centres could be more properly plan for cases with advanced disease by reducing the treatment intensity, thus reducing complications and more likely encouraging cases with terminal disease to be treated in hospices or at home [11], whereby their admission to hospital decreases, respectively [212, 213].

9.4.9.11 Bone marrow transplant

It is recommended that patients treated with radiotherapy as a part of a bone marrow transplant need to be followed up beyond five years after treatment completion [214]. This was highlighted because bone marrow transplant patients are at a higher risk of cancer recurrence than those who have not undergone such a procedure [214].

Neuroblastoma cases (25%) were the most likely to be treated with a BMT, followed by leukaemia (15%). After completion of cancer treatment, cases treated with a BMT had a significantly higher rate of admissions compared to cases who had not been treated with a BMT, after adjusting for age, sex, ethnicity, deprivation and type of initial treatment modality. Cases with a BMT had 54% higher admissions after completion of cancer treatment than cases who did not receive a BMT. Cases treated with a BMT and classified as receiving ‘some’ of their care at specialist units were found to have significant lower rates of admission after completion of treatment, compared to cases who received a ‘limited’ amount of specialist care.

9.4.9.12 Deceased patients

It was clear from the results of the literature review (Chapter 3), that there is very little information on hospital usage for those living with and beyond cancer, especially in terms of the effects of place of care, relapse status and type of treatment received during end of life care [152]. Understanding the range of services needed for those with terminal disease is vital for healthcare providers and commissioners, in order to plan services effectively. The aim was to identify whether the pattern of admissions differed among those who survived compared to deceased individuals. Deceased cases were analysed separately, as these individuals may represent a particular ‘high risk’ group of cancer patients, which may confound hospital activity analyses.

In this study, 21% of cases died during the follow-up period, and their median number of admissions increased from the date of diagnosis towards the last year of their life, such that the median number increased to nine admissions per person per year during the last year of life (Figure 48). This was supported by a systematic review based on 78 studies, that found that hospital admissions increased sharply near the date of death [152]. However, their study did not include children or young adults in their analysis. Therefore, the current analysis provides unique information on the CYP age range.

In the multivariable analysis, the ratio of admissions was similar according to patient characteristics for both the deceased and non-deceased groups. The only clear difference was for the volume of specialist care admissions, such that the non-deceased group had significantly higher admission rates among cases with higher levels of specialist care compared to cases with no specialist care, whilst among the deceased population, the rate of admission was significantly higher for those who received no specialist care. This could be explained by the fact that cases with more severe and advanced disease may be referred to palliative care services, so that care can be delivered in the home, rather than in the hospital setting. Cancer survivors that were transferred to specialist paediatric palliative care services had lower hospital admissions than those who were not, and this correlates with the decrease in the number of admissions for those who died during the follow-up period and received most of their care in specialist units [48].

Deceased individuals and those who relapsed had lower admissions when receiving the majority of their care in specialist cancer services, compared with those who received most of their care outside dedicated units. This suggests that specialist centres were more likely to provide care for those with a poor prognosis. Furthermore, these individuals might be more likely to be transferred to other healthcare settings that deal with terminal diseases, such as hospices. Future studies might therefore wish to look at hospital burden and the relationship between the level of specialist care and disease severity.

9.5 Clinical implications of the work

This sections include some recommendations based on the thesis key findings, to be addressed by healthcare providers and healthcare commissioners to provide appropriate services among the cancer cohort, and for patients and their families to cope with cancer and its related influence on their health, education and future career.

The hospital admissions for children and young people diagnosed with cancer and were linked to HES appeared to be slightly increased over time, ranging from 2% to 3% of

admissions in the period from 1997 to 2011 (Chapter 6), and the rate of admissions and length of stay significantly increased by diagnosis year (Chapter 7). This highlights an increased need for hospital resources in the future. Despite the results being tailored to cases diagnosed between 1996 and 2009, this thesis is the first baseline clinical data on hospital admissions both during and after the treatment phase for CYP, and can be used as a benchmark for future studies both in the UK and internationally.

The study highlighted the characteristics that can impact upon the risk of admission and length of stay. These were summarised as follows: 1) Children had higher rates of admissions and stayed for longer periods in hospital than TYAs for all cancers combined; 2) females had significantly longer hospital stays than males when diagnosed with leukaemia; 3) South Asians with STS had significantly lower hospital admissions and shorter lengths of stay than non-South Asians; 4) for all cancers combined, the most deprived cases had the highest hospital admissions and longest hospital stays, and that was significant among CNS cases; 5) cases receiving mostly specialist admissions were likely to stay for longer periods in hospital than cases receiving limited specialist admissions, demonstrating a disproportion in hospitalisation use by place of care; 6) cases with relapsed disease had a greater risk of hospitalisation and stayed for longer periods in hospital compared with non-relapsed cases, and that difference was present one year after date of diagnosis, especially for lymphoma cases and bone tumour cases although the rate of admissions sharply decreased after the date of the relapse, those cases were at continuous risk of hospitalisation, even four years after relapse; 7) bone tumour and leukaemia cases represented the tumour groups with the highest level of hospital activity for both children and TYAs – healthcare providers in Yorkshire need to be aware of the hospital burden among CYP diagnosed with bone tumours and leukaemia in particular. Future studies should attempt to identify the causes of the increase in admissions by looking at national cancer registry and linked HES data. The effect on survival and other health outcomes from those receiving different levels of specialist care especially for TYA should also be investigated in the future more closely to try to explain the finding of higher rates of admissions and a longer hospital stay associated with those having a higher proportion of their care in specialist settings. The ongoing BRIGHTLIGHT study may provide answers to some of these questions [216].

Healthcare commissioners need to ensure that capacity exists within their local clinical teams to meet the needs of these individuals. Dealing effectively with any treatment-related effects resulting in a hospital admission will have a benefit to young cancer survivors, given the potential life years to be gained in living beyond childhood and young adulthood.

The level of specialist care received was found to impact upon health outcomes among TYA survivors in earlier studies [8]. In this thesis, the CYP outcome was similarly impacted by the specialist centre, from the date of diagnosis throughout the follow-up period, where cases treated in specialist centres had higher rates of admissions and longer lengths of stay for all cancers combined. However, TYAs received lower levels of specialist care than children, this increases awareness of the fact that TYAs still lack centralised services. This finding could feed in to the BRIGHTLIGHT (www.brightlightstudy.com) objectives, by providing an evidence-based study emphasising the continuous work needed to allocate centralised services for TYAs aged 15-29. BRIGHLIGHT is a national collaboration focusing on assessing the impact of specialist centres on TYA outcomes.

Deceased cases had the highest median number of admissions one year prior to death (Chapter 6), and the rate of admissions was lower among cases treated mostly in specialist centres than cases with limited specialist care (Chapter 7). This highlights the fact that treating cases with terminal illness in specialist centres reduces hospital admissions, thus specialist centres have the advantage of providing CYP with a better quality of life after being diagnosed with cancer. This is evidenced by earlier work in Yorkshire, which assessed the impact of specialist palliative care in reducing hospital admissions among childhood survivors aged 0-19 and diagnosed between 1990 and 2009 [48]. Therefore, collaboration between professionals, including healthcare providers (doctors) and commissioners, is necessary to implement regulations to ensure that CYP with terminal illness are referred to specialist palliative care services or hospices to reduce unnecessary admissions, as this allows patients to be treated at home with the availability of 24/7 nursing support, thus personal, economic and social benefits might be attained by such cases.

Most of the cancer epidemiological studies focused on cancer's late effects using five-year survival outcomes as a cut-off point indicative of 'cure', irrespective of treatment modality or duration [15, 71, 101, 140, 150]. Using the arbitrary five-year survival could hide the true burden of health among survivors after completing their treatment – 12,474 admissions in this thesis occurred after treatment completion within five-years of diagnosis, which might be omitted in the analysis in earlier published studies. Additionally, the treatment duration varies by cancer type, where leukaemia cases often require up to three years of chemotherapy treatment, whilst some CNS tumours require 18 to 27 months of chemotherapy and/or radiotherapy [79]. The *Teenagers and Young Adults with Cancer* (TYAC) group includes multi-disciplinary professionals, and was established in 2004 with the aim of improving quality of life among young people with cancer at a national level. This group, in 2014, highlighted the importance of the availability of a

detailed summary of the treatment plan, including date of treatment completion from every healthcare centre, to provide young people with cancer with a better quality of life, by supporting the patient after the end of treatment. This also allows them to assess the influence of treatment change on patient outcome, in terms of length of stay and survival rate after treatment is completed. This thesis is the first health services study to estimate approximate treatment duration by cancer type, hence, assign date of treatment completion for each case. This provide a more accurate estimate of hospital admissions occurring during and after treatment completion, where it was found that the majority of admissions occurred during the first three years after treatment completion (Chapter 6). Therefore, this thesis has identified a critical phase in the care pathway for survivors immediately after the end of their main treatment phase, resulting in a significant burden on secondary care services, and supports further health services research to establish the causes of these hospitalisations. However, the estimation of date of treatment completion was tailored to the specific cancer types due to the limited number of cases, hence this needs to be replicated at a national level to include more cases sufficient to assess the impact of treatment changes on hospital usage among all cancers occurring among CYP.

Finally, a third of the cases were admitted at least once after treatment completion, and had double the rate of admissions compared to the background population after completion of cancer treatment. The majority of cases were related to diseases of the blood, neoplasms and endocrine diseases. Leukaemia survivors had the highest rate of admissions than other cancer groups and was six-times higher among children than TYAs, apart from endocrine diseases. Females had the highest excess rate of endocrine illness compared to males after treatment completion. Health strategies need to be issued to encourage TYAs, along with children, to take part in short- and long-term health surveillance, particularly for endocrine and metabolic diseases, and to increase awareness among survivors and their healthcare providers to ensure appropriate services are available to improve survivors' quality of life beyond cancer.

9.6 Strengths

A key strength was the ability to extract data from a population-based cancer register with high levels of case ascertainment and with active follow-up every two years for almost all current survivors (0.8% lost to follow-up, [172]). Details included relapse, recurrence of malignancy, death and any subsequent treatment. A unique feature of the cancer register is the inclusion of all newly diagnosed cases aged up to 30 years, providing important new information on hospital activity patterns within the entire childhood, teenage and young adult age range.

Electronic linkage of cases between the cancer registry and hospital records allowed an efficient and comprehensive analysis on health burden to be described. Most previous reports on health outcomes from the epidemiological research literature have mainly emerged from two large-scale retrospective cohort studies: the Childhood Cancer Survivorship Study (CCSS) in the United States [12, 147], and the British Childhood Cancer Survivorship Study (BCCSS) [217]. Information on survivors' late comorbidity was extracted from self-reported questionnaires, in contrast to this thesis. Data gained from questionnaires pertaining to long-term survivors is prone to recall bias and is likely to be subjective, whilst data drawn from administrative sources tend to be more objective, and relatively consistent between hospital attendees.

Individuals treated in PTCs should be treated according to recognised national clinical guidelines and standards [11]. However, there will be more heterogeneity within the TYA age group since a higher proportion were/will be treated outside of PTCs. So, results should be reasonably generalizable for the study population of 0-24 year olds seen within PTCs. Additionally, cases were extracted from a single population-based specialist childhood and young adult cancer register that used multiple sources of ascertainment [159], thus minimising any selection bias or any duplication of cancer registrations.

There was a small but limited published literature on hospital admissions describing the health burden among children and young adults with cancer [15, 22, 23, 70, 79, 87, 101, 140, 148-150], and none assessed health burden specifically following the date of diagnosis and date of treatment completion. Therefore, this thesis has strength in providing new evidence on the burden of healthcare activity associated with cancer treatment in young people both during treatment and after its completion. The published literature either assessed the paediatric or TYA age group [23, 87], but not the entire 0-29 year population, or specific cancer types, or related consequences [22, 79, 148]. Additionally, their analyses were limited to long-term cancer-related comorbidities [15, 101, 140, 148, 150].

9.7 Limitations

This thesis provided comprehensive and original findings of the hospital services burden among CYP in Yorkshire, from date of diagnosis, through treatment, and after treatment completion. The factors that influence hospital admissions and length of stay were identified, and the excess risk of morbidity, compared with the background population, was described based on cancer type, age at diagnosis and gender. However, there are limitations of the study that need to be considered.

The cases in this study were extracted from a population-based cancer register, including 3,447 cases diagnosed between 1996 and 2009; 96% were successfully electronically linked to at least one hospital record. The characteristics of the unlinked cases were not statistically different to the linked cases in terms of the distribution of cancer type, gender and deprivation score. However, there were significant differences by year of diagnosis, with cases who were diagnosed in the earlier period more likely to be unlinked, which might limit the study power and bias the result. This could be as a result of linkage errors, however any mismatch linkage would be less likely to occur as the linkage was based upon four separate patient identifiers: NHS number, date of birth, sex and postcode at the time of diagnosis. Additionally, some of the linked cases were eliminated from the study as they were not admitted after diagnosis i.e. all their admissions occurred before the recorded date of diagnosis. This could denote documentation errors in the cancer register based upon information extracted from the medical notes as certain cases might have a delayed entry of date of diagnosis due to the time taken for histopathological confirmation. Consequently, this could lead to an underestimation of the total burden of hospital admissions among the cancer cohort. However, such cases represented only 5% of total linked cases and their socioeconomic status was not significantly different from those which were linked and included in the analyses.

Despite the cancer register ascertaining childhood cases (ages 0-14 years) diagnosed as far back as 1974, the current study was limited to those diagnosed since 1996, due to the appropriate quality of linked HES data emerging at that time. This could limit the ability to assess hospital burden among extremely long-term childhood and young adult cancer patients and survivors. Data not analysed showed that cases diagnosed before 1996 were less likely to be linked, which could bias the analysis of the trend in hospital admission levels over time. Additionally the hospital burden were assessed from 1997 based on the available linked data, hence admissions occurred among cases diagnosed in 1996 might be underestimated.

The study included 3,151 individuals with cancer and with hospital linkages, who were responsible for 61,971 admissions. There have been some smaller [140, 150], and larger sized published studies on hospital activity levels among children and young people with cancer [101, 149]. Treatment was grouped according to all possible combinations (surgery, chemotherapy, radiotherapy, BMT) based on information recorded in the YSRCCYP. This is likely to be accurate and complete as all initial treatment is abstracted directly from medical records and cases are proactively followed-up every 2 years to determine whether any subsequent treatment has been administered. However, a small minority of leukaemia cases were found to be treated with surgery alone without any chemotherapy and these were re-checked by the YSRCCYP data manager.

The study might be limited as a result of grouping cases into two age groups: children aged 0-14 years and young adults aged 15-29 years. This might not necessarily coincide with natural distinctions in place of care, as some older adolescents may be treated in paediatric settings and vice versa. Furthermore, the age boundary for separating children from teenagers and young adults varied widely in the literature [2, 8, 23, 36, 70, 71]. However, this cut off point did provide an equal distribution in the span of age, yielding a sufficient number of cases for comparative purposes.

The main outcome investigated differences in age according to two age groups: children, and teenagers and young adults. This was done based on potential differences in management of treatment, in terms of place of care and type of treatment received. However, a single classification scheme of cancer was used (the ICCC [46]), rather than a specific TYA classification scheme [38], this facilitated relevant internal comparisons by main diagnostic group and also minimised the percentage of cases classified as 'other' (0.1% using ICCC and 2.0% for Birch [49]).

The documentation of some individual's sociodemographic characteristics (e.g. ethnicity) and clinical characteristics (e.g. type of initial treatment) was often poorly or inconsistently recorded in the UK within healthcare settings. This was evident from the analysis of HES data linked to the cancer register. The limitation in the recording of these variables was overcome in the following ways:

The documentation of ethnicity was validated using multiple resources: the cancer register, HES, and name recognition software (Chapter 4) [173, 174, 176]. Cases were grouped according to South Asians and non-South Asians, reflecting the largest ethnic minority population in Yorkshire, mainly originating from Mirpur in rural Pakistan [59].

Furthermore, the incompleteness in recording of the initial type of treatment was addressed and supplemented by linking HES to the cancer register. Nevertheless, some cancer types such as leukaemia cases were recorded as having surgery alone and that was not clinically accurate, highlighting possible documentation error in the data sources or incompleteness of recording of treatment and this was for limited number of cases. The date of treatment completion was not documented consistently in the cancer register for each patient nor was it available within the linked HES data. This was resolved by using a bespoke measure of treatment duration based on clinical expertise, after identifying the type of initial treatment and tumour diagnosis, using a novel matrix designed specifically for children and TYAs (Chapter 4, section 4.11.4, pages 91-). Furthermore, only major surgical procedures were included (so any minor or inconsequential interventions, such as diagnostic procedures, were excluded) to ensure that only cancer-related treatment was considered. This allowed the study to provide new information on the hospital burden during the expected treatment phase from the

point of diagnosis. Although this measure is more precise than simply using a standard cut-off of five years from diagnosis as many previous studies have used [101, 140, 150], it was still imperfect, as it was also based on an arbitrary cut-off point, assuming a similar duration of treatment for cases based on the same treatment modality and cancer type, therefore there will be some inaccuracy in the treatment duration and therefore the interpretation of findings need to be considered with some caution.

The results describing hospital burden could also be influenced by stage, grade or other disease severity measures which were not consistently recorded in the cancer register and therefore were not directly adjusted for in the regression modelling. Additionally, stage of disease might influence the type of initial treatment administered and would influence hospitalisation rates and length of stay. However, causal inference theory specifically precludes adjustment of covariates which occur on the casual pathway as this would bias the regression coefficients [218]. Therefore in this study it would be invalid to adjust for both stage and initial treatment stage when the outcome is hospital burden (or length of stay). Initial treatment was more accurately and completely recorded on the register than stage, therefore the former was included in the model without stage. Thus any effect of stage on the results is likely to be mitigated by adjusting for initial treatment. Future work, however, should be done to compare the regression modelling results using stage in place of initial treatment to assess its direct influence on hospital activity, once data quality for stage has been improved.

The diagnosis or the cause of admission was documented at different levels within HES, in terms of being either the primary or secondary cause. The primary cause should be that identified as the main reason for admission, while a secondary diagnosis could be another disease that relates to the primary cause, but which is not the main reason for the patient being admitted to hospital (more detail is contained in Section 4.12.4). Restricting the analysis to consider primary causes only was not accurate in terms of measuring the total hospital burden among cancer survivors, as it would overestimate the burden of admissions for recurrent disease, while underestimating the cancer-related effects of other causes, such as respiratory illness. This could also lead to a potential recording limitation in HES, as most cancer patients would have their malignancy coded as the primary cause of admission, which could mask the actual burden due to other causes among this population. This highlights the importance in understanding the HES data structure and the quality of the coding before estimating hospital burden.

In this thesis, a natural comparison group was identified from an age-sex-period matched denominator population to estimate the excess rate of hospitalisation, derived from all HES admissions over a follow-up period matched to the Yorkshire register cohort (1997-2011). Estimation of excess hospitalisation rates could be biased towards the null by

comparing cancer survivors to the general population, some of whom may have a history of previous disease. From the founded literature some randomly selected a comparison group from a registry of health insurance [140], similarly others extracted a comparison group randomly from an administrative database that holds information on individuals who are permanent residents in the Netherlands [150], and both found an excess risk of hospitalisation among cancer survivors of 2.2 (95%CI:1.90–2.50), similar to the current finding of 2.4 (95%CI: 2.26-2.49). Selection bias might also be present as hospital activity was limited to information obtained from NHS healthcare providers (i.e. non-private hospitals), although this level of bias is likely to be small due to the high matching rates (96%) and the high proportion of young people referred to NHS providers for their cancer care and follow-up.

A degree of multiple testing was carried out on the same study population within similar subgroups which could result in increasing the possibility of type I decision errors through spurious statistically significant findings. Additionally, due to the small number of cases in some of the analyses, such as for BMT, results produced imprecise estimates with wide confidence intervals, so some degree of caution is required, particularly when making any clinical inferences.

Initially, it was planned to assess the relative risk of the total burden of admissions, i.e. multiple-admissions per patient adjusted for the background population denominator. However, flexible relative survival analyses, such as the Royston-Parmar model [219], which takes into account the difference in baseline hazard by adjusting for the population denominator, could not account for the multilevel structure of the data at the time of analysis.

The current study focused on inpatient activity with little information about outpatient activity, although the ratio of inpatient to outpatient admissions was 1:1.8. However, the level of detail associated with outpatient admissions was poor, especially the recording of causes or diagnoses during hospital visits, such that around 99.5% of hospital visits were coded as ‘factors influencing health’.

The study included cases diagnosed during 1996 to 2009, providing a retrospective cancer cohort, a period during which the management of treatment might have altered and could change also in the future. Despite all these caveats, this thesis documents the first comprehensive observational data on hospital activity patterns that can be used as a benchmark for future health services research studies.

9.8 Future work

As discussed in Section 9.5 above, : the date of treatment completion was a key variable derived in the current analyses, as to date there has been no published information on the health burden before and after treatment completion. Clearly, it would have been preferable and more accurate if the date of treatment completion was documented in the cancer registry for each individual, and this is something currently being undertaken at a national level, as a priority in work being overseen by the TYAC professional work. In this study, the information regarding treatment detail, such as dose and type of treatment administered were not included, due to the incomplete recording of these treatment details for both the cancer register and HES. It is encouraging for future studies that are investigating how hospital activity is affected by detailed type of treatment modality, i.e. the same treatment modality but with a more moderate dose, that in a few years' time, they will be able to link the national cancer registry dataset, Cancer Outcome and Services Dataset with other treatment national datasets such as the National Radiotherapy Dataset and Systemic Anti-Cancer Therapy Dataset (Chemotherapy), once the datasets have had time to mature in terms of quality and patient years.

Hospital activity (episodes) among individuals with cancer were followed-up in this study until 2011, based on the available data at the time of analysis. It will be useful to assess admissions beyond this date and complementary work has begun to exploit newly available data on HES admissions up to 2015 for the Yorkshire cohort, focusing on respiratory and mental health admissions. Assessment of the impact on hospital admission patterns through any recent changes in treatment management over the last five years would also be instructive.

All CYP diagnosed in the period 1996 to 2009 whilst living in the Yorkshire region were included in this population-based record-linkage study (assuming they had at least one hospital inpatient record). It found that bone tumour and leukaemia cases had the highest hospitalisation rates among children and TYAs, respectively. However, the numbers of cases within each main diagnostic group were limited due to the rarity of this disease in this age group, limiting the ability for subgroup analyses among tumours, such as lymphoblastic leukaemia, acute myeloid leukaemia and CNS embryonal tumours. This precluded analyses investigating detailed patterns according to sociodemographic and patient variables, including the presence of interaction effects. Nonetheless, a focus on these subgroups would be valuable as part of future work using national or international datasets.

The health burden was primarily based on health activity which took place in inpatient settings, which comprises a major proportion of the annual NHS budget [220]. However, alternative healthcare services which deal with short- and long-term survivors, such as primary care, were not considered. Future work could be done to expand the knowledge

of the healthcare burden associated with cancer accounting for care occurring away from inpatient settings.

In this study, the quantity of hospital activity was assessed across the childhood and young adult age group. However, it is also important to consider the psychological and emotional needs of young people during diagnosis, treatment, shortly after treatment completion and among long-term survivors. This would complement the current focus on quantifying hospital activity. The cost burden might also be helpful for healthcare commissioners and planners, especially as current UK government spending is being tightened.

9.9 Conclusion

In this study, a bespoke electronic patient-level linkage was used to assess the actual hospital burden and related morbidity of childhood and young adult cancer patients and survivors.

Childhood and young adult cancer survivors were at a sustained high risk of admissions compared to the age, sex and attained year of admission matched general population. A significant proportion presented with serious complications after completing cancer treatment resulting in subsequent hospitalisation. The rate of hospital admissions remained stable over time, however the rate of admissions increased more recently, partly due to changes in hospital episode recording methods. This study identified both the short- and long-term health effects among cancer survivors diagnosed as young people, yet have the potential to lead a long and healthy life, assuming sufficient healthcare services are in place to deal adequately with conditions that require hospitalisation.

Appendix A Recode of cancer types, and causes of admissions

Table A-I: Recording of cancer types based on Classification of Childhood Cancer.

Diagnostic group	Morphology	Topography	Recode
I. Leukemias, myeloproliferative diseases, and myelodysplastic diseases			
a. Lymphoid leukemias	9820, 9823, 9826, 9827, 9831–9837, 9940, 9948	C000-C809	11
b. Acute myeloid leukemias	9840, 9861, 9866, 9867, 9870–9874, 9891, 9895–9897, 9910, 9920,9931	C000-C809	12
c. Chronic myeloproliferative diseases	9863, 9875, 9876, 9950, 9960–9964	C000-C809	13
d. Myelodysplastic syndrome and other myeloproliferative diseases	9945, 9946, 9975, 9980, 9982–9987, 9989	C000-C809	14
e. Unspecified and other specified leukemias	9800, 9801, 9805, 9860, 9930	C000-C809	15
II. Lymphomas and reticuloendothelial neoplasms			
a. Hodgkin lymphomas	9650–9655, 9659, 9661–9665, 9667	C000-C809	21
b. Non-Hodgkin lymphomas (except Burkitt lymphoma)	9591, 9670, 9671, 9673, 9675, 9678–9680, 9684, 9689–9691, 9695,9698–9702, 9705, 9708, 9709, 9714, 9716–9719, 9727–9729,9731–9734, 9760–9762, 9764–9769, 9970	C000-C809	22
c.Burkitt lymphoma	9687	C000-C809	23
d. Miscellaneous lymphoreticular neoplasms	9740–9742, 9750, 9754–9758	C000-C809	24
e. Unspecified lymphomas	9590, 9596	C000-C809	25
III. CNS and miscellaneous intracranial and intraspinal neoplasms			
a. Ependymomas and choroid plexus tumor	9383, 9390–9394a	C000-C809	31
b. Astrocytomas	9380a, 9384, 9400–9411, 9420, 9421–9424, 9440–9442a	C72.3	32
c. Intracranial and intraspinal embryonal tumors	9470–9474, 9480, 9508a	C70.0–C72.9	33
	9501–9504a	C000-C809	33

Diagnostic group	Morphology	Topography	Recode
d. Other gliomas	9380a	C70.0–C72.2, C72.4–C72.9,C75.1, C75.3	34
	9381, 9382, 9430, 9444, 9450, 9451, 9460a		34
e. Other specified intracranial and intraspinal neoplasms	8270–8281, 8300, 9350–9352, 9360–9362, 9412, 9413, 9492, 9493,9505–9507, 9530–9539, 9582a	C000-C809	35
f. Unspecified intracranial and intraspinal neoplasms	8000–8005a	C70.0–C72.9, C75.1–C75.3	36
IV. Neuroblastoma and other peripheral nervous cell tumours			
a. Neuroblastoma and ganglioneuroblastoma	9490, 9500	C000-C809	41
b. Other peripheral nervous cell tumours	8680–8683, 8690–8693, 8700, 9520–9523	C000-C809	42
	9501–9504	C00.0–C69.9, C73.9–C76.8,C80.9	42
V. Retinoblastoma	9510–9514	C000-C809	51
VI. Renal tumours			
a. Nephroblastoma (Wilms' tumour) and other nonepithelial renal tumours	8963	C64.9, C80.9	61
	8959, 8960, 8964–8967, 9364	C64.9	61
b. Renal carcinomas	8010–8041, 8050–8075, 8082, 8120–8122, 8130–8141, 8143, 8155,8190–8201, 8210, 8211, 8221–8231, 8240, 8241, 8244–8246,8260–8263, 8290, 8310, 8320, 8323, 8401, 8430, 8440, 8480–8490, 8504, 8510, 8550, 8560–8576	C64.9	62
	8311, 8312, 8316–8319, 8361	C000-C809	62
c. Unspecified malignant renal tumours	8000–8005	C64.9	63
VII. Hepatic tumours			
a. Hepatoblastoma	8970	C000-C809	71
b. Hepatic carcinomas	8010–8041, 8050–8075, 8082, 8120–8122, 8140, 8141, 8143, 8155,8190–8201, 8210, 8211, 8230, 8231, 8240, 8241, 8244–8246,8260–8264, 8310, 8320, 8323, 8401, 8430, 8440, 8480–8490,8504, 8510, 8550, 8560–8576	C22.0, C22.1	72
	8160–8180	C000-C809	72
c. Unspecified malignant hepatic tumours	8000–8005	C22.0, C22.1	73
VIII. Malignant bone tumours			

Diagnostic group	Morphology	Topography	Recode
a. Osteosarcomas	9180–9187, 9191–9195, 9200	C40.0–C41.9, C76.0–C76.8,C80.9	81
b. Chondrosarcomas	9210, 9220, 9240	C40.0–C41.9, C76.0–C76.8,C80.9	82
	9221, 9230, 9241–9243	C000-C809	82
c. Ewing tumour and related sarcomas of bone	9260	C40.0–C41.9, C76.0–C76.8,C80.9	83
	9363–9365	C40.0–C41.9	83
d. Other specified malignant bone tumours	8810, 8811, 8823, 8830,8812, 9250, 9261, 9262, 9270–9275, 9280–9282, 9290, 9300–9302,9310–9312, 9320–9322, 9330, 9340–9342, 9370–9372	C40.0–C41.9	84
e. Unspecified malignant bone tumours	8000–8005, 8800, 8801, 8803–8805	C40.0–C41.9	85
IX. Soft tissue and other extraosseous sarcomas			
a. Rhabdomyosarcomas	8900–8905, 8910, 8912, 8920, 8991	C000-C809	91
b. Fibrosarcomas, peripheral nerve sheath tumours, and other fibrous neoplasms	8810, 8811, 8813–8815, 8821, 8823, 8834–8835	C00.0–C39.9, C44.0–C76.8,C80.9	92
	8820, 8822, 8824–8827, 9150, 9160, 9491, 719540–9571, 9580	C000-C809	92
c. Kaposi sarcoma	9140	C000-C809	93
d. Other specified soft tissue sarcomas	8587, 8710–8713, 8806, 8831–8833, 8836, 8840–8842, 8850–8858,8860–8862, 8870, 8880, 8881, 8890–8898, 8921, 8982, 8990,9040–9044, 9120–9125, 9130–9133, 9135, 9136, 9141, 9142,9161, 9170–9175, 9231, 9251, 9252, 9373, 9581, 8830	C00.0–C39.9, C44.0–C76.8,C80.9	94
	8963	C00.0–C63.9, C65.9–C69.9,C73.9–C76.8, C80.9	94
	9180, 9210, 9220, 9240	C49.0–C49.9	94
	9260	C00.0–C39.9, C47.0–C75.9	94
	9364	C00.0–C39.9, C47.0–C63.9,C65.9–C69.9, C73.9–C76.8, C80.9	94
	9365	C00.0–C39.9, C47.0–C63.9,C65.9–C76.8, C80.9	94
e. Unspecified soft tissue sarcomas	8800–8805	C00.0–C39.9, C44.0–C76.8	95
X. Germ cell tumours, trophoblastic tumours, and neoplasms of gonads			
a. Intracranial and	9060–9065, 9070–9072, 9080–	C70.0–C72.9, C75.1–	101

Diagnostic group	Morphology	Topography	Recode
intraspinal germ cell tumours	9085, 9100, 9101a	C75.3	
b. Malignant extracranial and extragonadal germ cell tumours	9060–9065, 9070–9072, 9080–9085, 9100–9105	C00.0–C55.9, C57.0–C61.9,C63.0–C69.9, C73.9–C63.0–C69.9, C73.9–C75.0, C75.4–C76.8,C80.9	102
c. Malignant gonadal germ cell tumours	9060–9065, 9070–9073, 9080–9085, 9090, 9091, 9100, 9101	C56.9, C62.0–C62.9	103
d. Gonadal carcinomas	8010–8041, 8050–8075, 8082, 8120–8122, 8130–8141, 8143, 8190–8201, 8210, 8211, 8221–8241, 8244–8246, 8260–8263, 8290,8310, 8313, 8320, 8323 8380–8384, 8430, 8440, 8480–8490, 8504, 8510, 8550, 8560–8573, 9000, 9014, 9015,	C56.9, C62.0–C62.9	104
	8441–8444, 8450, 8451, 8460–8473	C000-C809	104
e. Other and unspecified malignant gonadal tumours	8590–8671	C56.9, C62.0–C62.9	105
	8000–8005	C000-C809	105
XI. Other malignant epithelial neoplasms and malignant melanomas	8370–8375		
a. Adrenocortical carcinomas			111
b. Thyroid carcinomas	8010–8041, 8050–8075, 8082, 8120–8122, 8130–8141, 8190, 8200,8201, 8211, 8230, 8231, 8244–8246, 8260–8263, 8290, 8310,8320, 8323, 8430, 8440, 8480, 8481, 8510, 8560–8573	C73.9	112
	8330–8337, 8340–8347, 8350	C000-C809	112
c. Nasopharyngeal carcinomas	8010–8041, 8050–8075, 8082, 8083, 8120–8122, 8130–8141, 8190,8200, 8201, 8211, 8230, 8231, 8244–8246, 8260–8263, 8290,8310, 8320, 8323, 8430, 8440, 8480, 8481, 8500–8576	C11.0–C11.9	113
d. Malignant melanomas	8720–8780, 8790	C000-C809	114
e. Skin carcinomas	8010–8041, 8050–8075, 8078, 8082, 8090–8110, 8140, 8143, 8147,8190, 8200, 8240, 8246, 8247, 8260, 8310, 8320, 8323, 8390–8420, 8430, 8480, 8542, 8560, 8570–8573, 8940, 8941	C44.0–C44.9	115
f. Other and unspecified carcinomas	8010–8084, 8120–8157, 8190–8264, 8290, 8310, 8313–8315, 8320–8325, 8360, 8380–8384, 8430–8440, 8452–8454, 8480–8586,8588–8589, 8940, 8941, 8983, 9000, 9010–9016, 9020, 9030	C00.0–C10.9, C12.9–C21.8,C23.9–C39.9, C48.0–C48.8, C50.0–C55.9,C57.0–C61.9, C63.0–C63.9, C65.9–C72.9,C75.0–C76.8, C80.9	116

Diagnostic group	Morphology	Topography	Recode
XII. Other and unspecified malignant neoplasms			
a. Other specified malignant tumours	8930–8936, 8950, 8951, 8971–8981, 9050–9055, 9110	C00.0–C39.9, C47.0–C75.9	121
	9363	C000-C809	121
b. Other unspecified malignant tumours	8000–8005	C00.0–C21.8, C23.9–C39.9,C42.0–C55.9, C57.0–C61.9, C63.0–C63.9,C65.9–C69.9, C73.9–C75.0, C75.4–C80.9	122
Not classified by ICCC or in situ			999

ICD-O-3: International Classification of Diseases for Oncology, third edition;
CNS: central nervous system
a: Tumours with non-malignant behaviour are included for all morphology codes on the line: [209]

Table A-II: Recoding of causes of admissions based on ICD-10 codes.

Analysis code	ICD codes	Definition
1	A00-B99	Certain infectious and parasitic diseases
2	C00-D48	Neoplasms
3	D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
4	E00-E90	Endocrine, nutritional and metabolic diseases
5	F00-F99	Mental and behavioural disorders
6	G00-G99	Diseases of the nervous system
7	H00-H59	Diseases of the eye and adnexa
8	H60-H95	Diseases of the ear and mastoid process
9	I00-I99	Diseases of the circulatory system
10	J00-J99	Diseases of the respiratory system
11	K00-K93	Diseases of the digestive system
12	L00-L99	Diseases of the skin and subcutaneous tissue
13	M00-M99	Diseases of the musculoskeletal system and connective tissue
14	N00-N99	Diseases of the genitourinary system
15	O00-O99	Pregnancy, childbirth and the puerperium
16	P00-P96	Certain conditions originating in the perinatal period
17	Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities
18	R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
19	S00-T98	Injury, poisoning and certain other consequences of external causes
20	V01-Y98	External causes of morbidity and mortality
21	Z00-Z99	Factors influencing health status and contact with health services
22	U00-U99	Codes for special purposes

Appendix B List of diagnostics and supportive surgeries: main surgeries extracted from the cancer register and HES

Table B-I: List of diagnostics and supportive surgeries extracted from the cancer register

Operation code	Code Description
P5599	Abdominal operations, not elsewhere classified - biopsy
P0579	Biopsy of brain
P3870	Biopsy of breast
P3879	Biopsy of breast
P8290	Biopsy of buttock
P7069	Biopsy of cervix
P9209	Biopsy of skin and subcutaneous tissue
P3409	Bronchoscopy with biopsy
P9641	Endoscopy, not elsewhere classified - with biopsy, not elsewhere classified
P4501	Enterotomy - biopsy, not elsewhere classified
P9531	Excision - biopsy, not elsewhere classified
P0801	Excision of cervical lymph nodes - biopsy (scalene node)
P8321	Excision of lesion of muscle, biopsy
P5501	Exploration and drainage of peri-renal tissue - biopsy
P5629	Exploration of renal pelvis - biopsy
P4311	Gastric intubation with related procedures - biopsy of duodenum, jejunum
P4319	Gastric intubation with related procedures - endoscopy, gastroscopy
P4319	Gastric intubation with related procedures - endoscopy, gastroscopy
P4269	Gastro-enterostomy
P4701	Incision of rectum, biopsy
P6409	Incision of testis and adnexa - biopsy
P2611	Incision of tongue - biopsy of tongue
P3304	Incision or puncture of chest wall - thoracoscopy
P0206	Laminotomy and laminectomy - biopsy of bone
P4022	Laparotomy - biopsy (abdominal) (peritoneal)
P4023	Laparotomy - exploratory
P5019	Needle biopsy - punch biopsy
P5601	Nephrotomy, not elsewhere classified - exploration
P5602	Nephrotomy, not elsewhere classified - biopsy
P0401	Neurectomy and neurotomy - biopsy
P2941	Oesophagoscopy - with biopsy
P3354	Operations of mediastinum - biopsy
P3474	Operations upon bronchus, not elsewhere classified - biopsy
P1001	Orbitotomy, biopsy of orbit
P1891	Other operation on eye - biopsy of eye, not otherwise stated
P7399	Other operation on female genital organs - biopsy of labia, perineum, vulva, clitoris
P2671	Other operation on mouth and palate - biopsy - faeces, palate
P2399	Other operation on nasopharynx, biopsy
P9299	Other operation on skin or subcutaneous tissue, not elsewhere classified, biopsy
P6591	Other operation on testis and adnexa - biopsy

P0691	Other operations on adrenal gland - biopsy
P3391	Other operations on chest - biopsy
P2091	Other operations on ear, not elsewhere classified - biopsy
P3099	Other operations on heart-not elsewhere classified - cardioscopy
P8221	Other operations on joints or cartilage - biopsy
P5091	Other operations on liver, open biopsy
P2241	Other operations on nose and face, biopsy
P4051	Other operations on omentum and mesentery - biopsy
P6791	Other operations on ovary - biopsy
P1691	Other operations on retina, or choroid - biopsy of retina or choroid
P2754	Other operations on salivary gland and duct - biopsy
P0091	Other operations on skull and meninges, biopsy
P0291	Other operations on spine and contents - biopsy of cord or meninges
P0711	Partial thyroidectomy - biopsy
P5641	Percutaneous puncture of kidney - biopsy
P9541	Puncture - percutaneous biopsy, not elsewhere classified
P7981	Puncture of bone - biopsy of bone
P7982	Puncture of bone - biopsy of marrow
P4681	Sigmoidoscopy - with biopsy
P0019	Craniotomy, not elsewhere classified - decompression, exploration, biopsy
P0803	Excision of cervical lymph nodes - radical cervical
P0806	Excision of cervical lymph nodes - simple excision
P0809	Excision of cervical lymph nodes, not elsewhere classified
P9059	Lymphatic biopsy, not elsewhere classified
P6081	Cystoscopy - biopsy

Table B-II: List of diagnostics and supportive surgeries extracted from HES

Operation code	**Code description**
A013	Biopsy of the brain
A045	Open biopsy of lesion of tissue of brain
A085	Other biopsy of lesion of tissue of brain
A559	Diagnostic spinal puncture
C861	Biopsy of lesion of eye neck
E095	Biopsy of lesion of external nose
E271	Open biopsy of lesion of pharynx
E381	Diagnostic endoscopic examination of larynx
E491-9	Diagnostic fibrotic endoscopic examination on lower respiratory tract
E593	Biopsy of lesion of lung neck
E631	Diagnostic endoscopic examination of mediastinum
F091	Surgical removal of tooth
F115	End osseous implantation into jaw
F135	Restoration of part of tooth using filing neck
F145	Surgical exposure of tooth
F164	Scaling of tooth
F172	Operation of teeth using dental crown
F189	Excision of dental lesion of jaw

F201	Operations on gingiva
F238	Extrication of lesion of tongue
F263	Other operation on tongue
F342-8	Excision of osil
G152-9	Other therapeutic fibrotic endoscopic operations on oesophagus
G218	Other operations on oesophagus
G241-3	Antireflux operations
G331	Other connection of stomach to jejunum
G344	Artificial opening into stomach
G451-9	Diagnostic fibrotic endoscopic examination of upper gastrointestinal tract
G478	Intubation of stomach
G484	Other operation of stomach
H011-9	Emergency excision of appendix
H131	Bypass of colon
H228	Diagnostic endoscopic examination of colon
H524	Destruction of haemorrhoid
J132	Diagnostic endoscopic examination of liver
J439	Diagnostic endoscopic retrograde examination of bile duct pancreatic duct
K635	Constrict radiology of heart
K651-9	Catheterisation of heart
L941	Therapeutic transluminal operations on vein
M113	Diagnostic endoscopic examination of kidney
M451-9	Diagnostic endoscopic examination of bladder
N134	Biopsy of testis
N321	Biopsy of lesion of penis
P091	Biopsy of lesion of vulva
Q034	Biopsy of cervix uteri
Q034	Punch biopsy of cervix uteri
Q181-9	Diagnostic endoscopic examination of uterus
Q188	Diagnostic endoscopic examination of uterus
Q553	Other examination of female genital tract
R053	Diagnostic percutaneous examination of foetus
R151	Other induction of labour
R182	Other caesarean delivery
R215	Forceps cephalic delivery
R229	Vacuum delivery
R232	Cephalic vaginal delivery with abdominal presentation of head at delivery without instrument
S132	Punch biopsy of skin
S151-9	Other biopsy of skin
S551	Exploration of burnt skin of other site
S563	Exploration of other skin of head or neck
S571	Exploration of skin other site
T111	Diagnostic endoscopic examination of pleura
T122-9	Puncture of pleura
T431-9	Diagnostic endoscopic examination of peritoneum

T813	Biopsy of muscle
T861	Sampling of lymph nodes
T911	Biopsy od sentinel lymph node neck
U011	Diagnostic imaging of whole body
U051-9	Diagnostic imaging of central nervous system
U063	Diagnostic imaging of face and neck
U071	Diagnostic imaging of chest
U081-9	Diagnostic imaging of abdomen
U092-9	Diagnostic imaging of pelvis
U121-9	Diagnostic imaging of genitourinary system
U133	Diagnostic imaging of musculoskeletal system
U202	Diagnostic echocardiography
U211-9	Diagnostic imaging procedures
U221	Neuropsychology test
U261	Diagnostic testing of genitourinary system
U291-9	Diagnostic endocrinology
U301	Autonomic cardiovascular testing
U321-9	Diagnostic blood tests
U331	Other diagnostic tests
U354	Other diagnostic imaging of vascular system
U372	Other diagnostic imaging of genitourinary system
V194	Biopsy of lesion of mandible
V478	Biopsy of spine
W361-9	Diagnostic puncture of bone
W879	Diagnostic endoscopic examination of knee joint
W941	Hybrid prosthetic replacement of hip joint using cemented acetabular component
X118	Amputation of toe
X123	Operations on amputation stump
X213	Correction of congenital deformity of hand
X222	Correction of congenital deformity of hip
X291-9	Continuous infusion of therapeutic substance
X301-9	Injection of therapeutic substance
X311-9	Injection of radiocontrast material
X323	Exchange blood transfusion
X331-9	Other blood transfusion
X348	Other intravenous transfusion
X352-9	Other intravenous injection
X361-9	Blood withdrawal
X373-9	Trans muscular injection
X381-9	Subcutaneous injection
X411-8	Placement of ambulatory apparatus for compensation for renal failure
X442	Administration of vaccine
X528	Oxygen therapy
X558	Other operations on unspecified organ
X591-9	Anaesthetic without surgery

X851	High cost neurology drugs
X861	Anti-effective drugs
X891-9	Immunosuppressant and urinary drugs
X893	High cost immunosuppressant drugs
X901-9	Haematology and nutrition drugs
X931	Ophthalmology drugs
X961-9	Immunology drugs
X381-5	Subcutaneous injection
X411	Placement of ambulatory apparatus for compensation for renal failure
X418	Placement of ambulatory apparatus for compensation for renal failure
X442	Administration of vaccine
X528	Oxygen therapy
X558	Other operations on unspecified organ
X598	Anaesthetic without surgery
X851	High cost neurology drugs
X893	High cost immunosuppressant drugs

Table B-III: List of major cancer-related surgeries extracted from the cancer register

Operation code	Operation description
P0011	Craniotomy - burr-hole
P0012	Craniotomy - trephine
P0014	Craniotomy - puncture of brain
P0049	Excision of lesion of skull
P0081	Ventricular puncture and anastomosis - drainage
P0083	Ventricular puncture and anastomosis - ventriculo-cisternostomy
P0084	Ventricular puncture and anastomosis - ventriculo-vascular anastomosis
P0089	Ventricular puncture and anastomosis
P0095	Other operations on skull and meninges - meningeal lesion
P0169	Revision or irrigation of ventricular shunt
P0172	Cranial puncture, not elsewhere classified-aspiration (brain substance, abscess)
P0201	Laminotomy and laminectomy - laminotomy
P0202	Laminotomy and laminectomy - excision of bone (tumour)
P0209	Laminotomy and laminectomy not elsewhere classified
P0262	Extirpation of intraspinal lesion - intradeduilary
P0269	Extirpation of intraspinal lesion, not elsewhere classified
P0289	Spinal puncture - nos
P0292	Other operations on spine and contents - removal of foreign body
P0293	Other operations on spine and contents - operation for spinal deformity
P0295	Other operation on spine and contents - aspiration (cyst, abscess)
P0402	Neurectomy and neurotomy - excision
P0499	Other operations on peripheral nerves
P0523	Operations on vessels of the brain - excision
P0554	Excision of intracranial lesion - frontal approach
P0559	Excision of intracranial lesion not elsewhere classified
P0591	Intracranial operations, - exploration
P0599	Intracranial operations, not elsewhere classified

P0633	Other operations related to pituitary or pineal gland - pineal
P0639	Other operations related to pituitary or pineal gland - not otherwise stated
P0659	Partial adrenalectomy
P0669	Excision of adrenal gland, not other classify. - adrenalectomy (transabdominal)
P0679	Bilateral adrenalectomy
P0712	Partial thyroidectomy - nodule
P0715	Partial thyroidectomy - lobectomy
P0716	Partial thyroidectomy, not elsewhere classified
P0719	Partial thyroidectomy
P0721	Thyroidectomy - total
P0729	Thyroidectomy, not elsewhere classified
P0759	Other operations on thyroid gland
P0899	Other operations in neck region, not elsewhere classified
P1019	Exenterating of orbit, not elsewhere classified
P1039	Removal of eyeball - enucleating (with implant)
P1699	Other Operations On Retina, Or Choroid - Destruction Of Lesion
P1899	Other operation on eye - suture of eyeball not elsewhere classified
P1919	Excision and destruction of external ear or lesion - open operation
P2019	Mastoidectomy and related bone exposure, not elsewhere classified
P2099	Other operations on ear neck
P2179	Excision of other lesions of nose and face
P2249	Other operations on nose and face
P2289	Drainage or excision nasal sinus not elsewhere classified
P2342	Tonsillectomy, not otherwise stated
P2349	Tonsillectomy
P2359	Adenoidectomy, not otherwise stated
P2361	Other operations on tonsil - removal foreign body
P2391	Other operation on nasopharynx, excision of lesion
P2439	Stripping vocal cords
P2479	Tracheotomy (temporary) not elsewhere classified
P2481	Tracheostomy and laryngectomy - external intubation
P2599	Other operations on teeth, gums, and jaws
P2669	Excision of soft tissue lesions of mouth, not elsewhere classified
P2701	Resection of salivary gland - total parotidectomy (radical)
P2702	Resection of salivary gland - conservative parotidectomy
P2841	Pharyngectomy and excision of lesion - partial pharyngectomy
P2842	Pharyngectomy and excision of lesion - excision of lesion
P3095	Other operations on heart, not elsewhere classified-repair heart or pericardium
P3301	Incision or puncture of chest wall - thoracentesis, not otherwise stated
P3302	Incision or puncture of chest wall - aspiration (air, fluid)
P3303	Incision or puncture of chest wall - drainage of pleural cavity (empyema)
P3309	Incision or puncture of chest wall
P3339	Repair of chest wall - miscellaneous
P3351	Operations of mediastinum - mediastinoscopy, not otherwise specified
P3352	Operations of mediastinum - mediastinotomy
P3353	Operations of mediastinum - excision or destruction of lesion
P3359	Operations of mediastinum
P3361	Operations upon pleura - decortication (thoracic)
P3364	Operations upon pleura - other pleurectomy

P3399	Other operations on chest - supra-sternal drainage, sternotomy
P3411	Bronchoscopy - aspiration
P3424	Incision or puncture of lung - puncture of lung
P3432	Excision, destruction lesion lung-resection bulla, cyst, bloc dissection bronchus
P3811	Partial mastectomy - excision of lesion (lumpectomy)
P3821	Mastectomy - simple mastectomy
P3829	Mastectomy- not elsewhere classified
P3891	Other operations on breast - aspiration of breast
P4001	Superficial operation of abdominal wall
P4029	Laparotomy not elsewhere classified
P4092	Operations On Abdominal Wall & Peritoneum-Incision Retroperitoneal, Urachal cyst
P4093	Other operations on abdominal wall and peritoneum - excision of lesion
P4099	Other operations on abdominal wall and peritoneum, not elsewhere classified
P4231	Partial gastrectomy - with oesophago-gastrostomy
P4269	Gastro-enterostomy
P4399	Other operations on stomach
P4522	Excision of small intestine or lesion - resection with re-anastomosis
P4523	Excision of small intestine or lesion - resection with enterostomy
P4529	Excision of small intestine or lesion not elsewhere classified
P4602	Colectomy and resection - with anastomosis
P4605	Colectomy and resection - excision colostomy mucosa
P4609	Colectomy and resection, not otherwise stated - caecectomy, hemicolectomy
P4619	Complete colectomy not elsewhere classified
P4669	Excision of lesion of large intestine - caecum, sigmoid, polypectomy of bowel
P4699	Other operations on intestine not elsewhere classified
P4711	Excision of rectum, not elsewhere classifed-abdominal-anal operation or anastomosis
P4712	Excision of rectum, not elsewhere classified-intra pelvic protectomy
P4739	Excision and destruction of lesion of rectum, not elsewhere classified
P4841	Other excision of anus or anal lesion - local excision of lesion
P4849	Other excision of anus or anal lesion - not otherwise specified
P4999	Other operations on anus
P5002	Hepatectomy - destruction of lesion
P5003	Hepatectomy - hemishepatectomy, lobectomy
P5005	Hepatectomy - liver transplant
P5009	Hepatectomy, not elsewhere classified
P5399	Other operations of pancreas
P5491	Other operations on spleen - splenectomy
P5591	Abdominal operations, not elsewhere classified - pelvic exenterating
P5659	Removal of kidney, complete - nephrectomy
P5671	Excision or destruction of lesion of kidney - partial nephrectomy
P5672	Excision or destruction of lesion of kidney - excision of cyst, tumour
P5799	Other operations on kidney, not otherwise specified
P6001	Cystectomy - stab cystectomy
P6009	Cystectomy - not elsewhere classified
P6021	Extirpation of lesion of bladder by open operation - partial cystectomy
P6023	Extirpation of lesion of bladder by open operation - excision of lesion

P6379	Other operations on prostate
P6402	Incision of testis and adnexa - incision of testis
P6403	Incision of scrotum and adnexa - removal of foreign body
P6419	Orchiectomy, unilateral or partial not elsewhere classified
P6471	Extirpation of lesion of scrotum or testis - scrotum
P6492	Repair of testis and adnexa - insertion of prosthesis
P6599	Other operation on testis and adnexa not elsewhere classified
P6719	Castration, female - bilateral oophorectomy
P6721	Partial oophorectomy - wedge resection
P6723	Partial oophorectomy - excision of lesion
P6729	Partial oophorectomy, not elsewhere classified
P6793	Other operations on ovary - oophorectomy, not elsewhere classified
P6799	Other operations on ovary
P6811	Salpinges- Oophorectomy - Unilateral
P6812	Salpinges- Oophorectomy - Bilateral
P6829	Salpingectomy
P6919	Extended hysterectomy
P6961	Hysterectomy, total
P6969	Hysterectomy, not elsewhere classified
P7002	Excision of lesion of uterus - polypectomy
P7009	Excision of lesion of uterus - not elsewhere classified
P7049	Curettage of uterus - dilation and curettage
P7059	Excision of lesion of cervix
P7099	Other operations on uterus
P7909	Incision of bone, removal of foreign body, drainage, drilling, exploration
P7929	Partial osteotomy not elsewhere classified
P7942	Excision of lesion of bone - exocytosis
P7949	Excision of lesion of bone
P7983	Puncture of bone - bone marrow transplant
P7998	Other operation on bone at other specified site
P7999	Other operations on bone, destruction, cryosurgery, curettage
P8011	Joint puncture aspiration/arthrocentesis
P8329	Excision of lesion of muscle
P8339	Excision of lesion of muscle - nec
P8619	Removal of upper limb, forequarter amputation, disarticulation at shoulder
P8629	Amputation of arm, through homeruns, at elbow
P8679	Other disarticulation, upper limb, not elsewhere classified
P8712	Amputation through thigh - above knee
P8719	Amputation through thigh
P8739	Amputation through lower leg - below knee - through malleoli
P8795	Other operations on limbs not elsewhere classified - foot
P8799	Other operations on limbs not elsewhere classified
P9039	Lymphatic excision not elsewhere classified
P9129	Excision of superficial cyst or fistula
P9131	Excision of other skin growth - wide excision
P9139	Excision of other skin growth, not elsewhere classified
P9141	Excision of other lesion of skin or subcutaneous tissue - wide excision
P9149	Excision of other lesion of skin or subcutaneous tissue-primary excision wound
P9159	Destruction of lesion of skin not elsewhere classified
P9169	Toilet of wound - debridement necessitating anaesthetic

P9599	Other operation with ill-defined site, not elsewhere classified
P0171	Cranial puncture, not elsewhere classified - needle biopsy of the brain

Table B-IV: List of major cancer-related surgeries extracted from HES

Operation code	Code discerption
A012-9	Major excision of lesion of brain
A038-9	Stereotactic ablation of tissue of brain
A051-4	Drainage of lesion of tissue of brain
A098	Neurostimulation of brain
A107	Other operation of tissue of brain
A113	Operations on tissue of brain
A131	Attention to component of connection from ventricle of brain
A139	Attention to component of connection from ventricle of brain
A171	Therapeutic endoscopic operations on ventricle of brain
A255	Intracranial transection of cranial nerve
A291-5	Excision of lesion of cranial nerve
A331	Neurostimulation of cranial nerve
A361	Other operation of cranial nerve
A383-9	Extrication of lesion of meninges of brain
A392-4	Repair of dura
A411-9	Drainage on subdural space
A422	Other operations on meninges of brain
A631	Other graft to peripheral nerve
A681	Other release of peripheral nerve
A709	Neurostimulation of peripheral nerve
A734	Exploration of peripheral nerve
B012-4	Excision of pituitary gland
B259	Other operation of adrenal tissue
B279	Total excision of breast
B284	Other excision of breast
B285-8	Other excision of breast
B295	Reconstruction of breast
B301	Prosthesis for breast
B311-2	Other plastic operation on breast
C012	Excision of eye
C021	Operation of lesion of orbit
C043-8	Attention to prosthetic of eye
C051	Plastic repair of orbit
C061	Incision of orbit
C111-8	Operation on canthus
C161	Other plastic repair of eyelid
C181-9	Correction of ptosis of eyelid
C191	Incision of eyelid
C311-9	Combined operations on muscles of eye
C326	Recession of muscle of eye

C332-6	Resection of muscle of eye
C345-6	Partial division of tendon of muscles of eye
C359	Other adjustment to muscle of eye
C378	Other operations on muscle of eye
C401	Repair of conjunctiva
C438	Other operations on conjunctiva
C452	Extrication of lesion of cornea
C468	Plastic operations on cornea
C828	Distraction of lesion of retina
C866	Examination of eye under anaesthetic
D063	Repair of external ear neck
D078	Clearance of external auditory canal
D131-4	Attachment of bone anchored hearing prosthesis
D151	Drainage of middle ear
D203	Other operation of middle ear
D241-3	Operations on cochlea
E018	Excision of nose
E333	Other open operations on larynx
E357	Other therapeutic endoscopic operations on larynx
E398	Partial excision of trachea
E429	Exteriorisation of trachea
F028	Extirpation of lesion of lip
F032-3	Correction of deformity of lip
F053	Other repair of lip
F363	Other operation on tonsil
F388	Extirpation of lesion of other part of the mouth
F409	Other repair of part of the mouth
F442-3	Other operation on mouth
F452	Extrication of lesion of salivary gland
G021	Total excision of oesophagus
G401	Incision of pylorus
G649	Therapeutic endoscopic operations on jejunum
H143	Exteriorisation of caecum
H299	Subtotal excision of colon
H333	Excision of rectum
H463	Other operations of rectum
H483	Excision of lesion of anus
H491	Destruction of lesion of anus
H608	Other operations on pilonidal
H628	Other operations on bowel
J021	Partial excision of liver
J273	Excision of bile duct
J388	Endoscopic incision of sphincter of duct
J575	Other partial excision of pancreas
J582	Extirpation of lesion of pancreas
J692	Total excision of spleen

J723	Other operations on spleen
K021	Other transplantation f heart
K192	Creation of other cardiac conduit
K571-2	Other therapeutic transluminal operations on heart
K661	Other operations on heart
K692	Incision of pericardium
L091	Other connection to pulmonary artery
L351	Transluminal operations on cerebral artery
L631	Transluminal operations on femoral artery
L773	Connection of vein cava or branch of vena cava
L793	Other operations on vena cava
L852	Ligation of varicose vein of leg
L918	Other vein related operations
M013	Transplantation of kidney
M021-3	Total excision of kidney
M042	Open extirpation of lesion of kidney
M051	Open repair of kidney
M094	Therapeutic endoscopic operations on calculus of kidney
M132	Percutaneous puncture of kidney
M149	Extracorporeal fragmentation of calculus of kidney
M261	Therapeutic nephoscopy operations on ureter
M271	Therapeutic ureteroscopic operations on ureter
M293	Other therapeutic removal of calculus from ureter
M362	Enlargement of bladder
M432	Endoscopic operations to in increase capacity of bladder
M494-8	Other operations on bladder
M523	Abdominal operations to support outlet of female balder
M582	Other operations on outlet of female bladder
M733	Repair of urethra
M768	Therapeutic endoscopic operations on urethra
N064	Excision of testicular appendage
N089	Bilateral placement of tests in scrotum
N132	Other operations on testis
N153	Operation on epididymis
N242	Operations on male perineum
N273	Extirpation of lesion of penis
Q024	Destruction of lesion of cervix uteri
Q071	Abdominal excision of uterus
Q078	Abdominal excision of uterus
Q233	Unilateral excision of adnexa of uterus
Q241	Other excision of adnexa of uterus
Q388	Other therapeutic endoscopic operations on fallopian tube
Q484	Oocyte recovery
Q493	Therapeutic endoscopic operations on ovary
Q558	Other examination of female genital tract
S069	Other excision of lesion of skin

S089	Curettage of lesion of skin
S179	Distal flap of skin and muscle
S308	Other operations of flap of skin to header neck
S315	Other operations of flap of skin to other site
S318	Other operations of flap of skin to other site
S433	Removal of repair material from skin
S442	Removal of other inorganic substance from skin
T013	Partial excision of chest wall
T201	Primary repair of inguinal hernia
T243	Primary repair of umbilical hernia
T273	Repair of hernia of abdominal wall
T288	Other repair of anterior abdominal wall
T311	Other operations on anterior abdominal wall
T312	Other operations on anterior abdominal wall
T418	Other open operations on peritoneum
T421-2	Therapeutic endoscopic operations on peritoneum
T461	Other drainage of peritoneal cavity
T501	Transplantation of fascia
T531	Excision of other fascia
T648	Transposition of tendon
T698	Freeing of tendon
T702	Adjustment of length of tendon
T723	Other operations on sheath of tendon
T761	Transplantation of muscles
T921	Other operations on lymphatic tissue
V011	Plastic repair of cranium
V092	Reduction of fracture of other bone of face
V131	Other operations on bone of face
V161	Division of mandible
V171	Fixation of mandible
V242	Decompression operations on thoracic spine
V439	Extirpation of lesion of spine
V543	Other operations on spine
W093-6	Extirpation of lesion of bone
W174	Other reconstruction of bone
W191-5	Primary open reduction of fracture of bone and intramedullary fixation
W205	Primary bone reduction of fracture of bone and extramedullary fixation
W241	Closed reduction of fracture of bone and internal fixation
W251	Closed reduction of fracture of bone and external fixation
W264	Other closed reduction of fracture of bone
W282	Other internal fixation of bone
W321	Other graft of bone
W336	Other open operations on bone
W341-9	Graft bone marrow
W593-5	Fusion of joint of toe
W611	Primary arthrodesis and articular bone graft neck

W693	Open operations on synovial membrane of joint
W742	Other reconstruction of ligament
W768	Other operations of ligament
W774-9	Stabilising operations on joint
W802	Debridement and irrigation of joint
W815	Other open operations on joint
W823	Therapeutic endoscopic operations on semilunar cartilage
W844	Therapeutic endoscopic operations on other joint structure
W919	Puncture of joint
Z921	Operation on head

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