The Long Term Mental Health of Survivors of Childhood and Young Adult Cancers

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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. Further details of jointly-authored publications and presentations are given below.

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Abstract

Since the 1970s, cancer in children and young people has become both increasingly common and more survivable. Whilst physical late effects of cancer are well documented, less is known about long-term mental health. A systematic review highlighted increased mental ill health amongst childhood and young adult cancer survivors. However, few studies included clinician-diagnosed mental health problems, and no population-based studies were found.

The Yorkshire Specialist Register of Cancer in Children and Young People was used to identify 7253 long-term survivors of early-life cancer. Records from routinely collected mental health data sets were used to identify individuals who had had contact with specialist mental health services, or who had a recorded mental health condition during an inpatient hospital stay. These were compared with population rates of specialist mental health services use and recorded mental health conditions, and standardised incidence ratios were calculated. Logistic regression was used to identify sub-groups at increased risk of mental health difficulties.

Cancer survivors were 73.7% more likely than the general population to have a recorded contact with specialist mental health services, but no more likely to have a recorded mental health diagnosis during an inpatient stay. Teenagers and young adults treated on specialist teenage and young adult units had more specialist mental health services contacts than those treated on standard wards.

The increased risk of mental health services use amongst cancer survivors should prompt clinicians to routinely enquire about mental health during contacts with this cohort. The increased risk amongst teenagers and young adults treated on specialist units was surprising, and it is unclear whether this represents a true increase in prevalence of mental ill health, or simply improved access to specialist services. Further work to understand the reasons behind increased mental health services use is essential, and should include analysis of primary care records.

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List of Abbreviations

15D	15 Dimensional Health Related Quality of Life Instrument
95% CI	95% Confidence Intervals
ALiCCS	Adult Life after Childhood Cancer in Scandinavia
ALL	Acute Lymphoblastic Leukaemia
AML	Acute Myeloid Leukaemia
ASPP	Assessment of Social Perspective-Taking Performance
ASR	Adult Self Report
AYA	Adolescents and Young Adults
BCCSS	British Childhood Cancer Survivors Study
BFS	Behaviour and Feeling Survey
BPI	Behaviour Problems Inventory
BSI	Brief Symptom Inventory
BSI-18	Brief Symptom Inventory (18 question form)
CBCL	Child Behaviour Checklist
CCSS	Childhood Cancer Survivors Study
CDI	Children’s Depression Inventory
CES-D	Centre for Epidemiological Studies – Depression Scale
CISS	Coping Inventory for Stressful Situations
CNS	Central Nervous System
CYP	Children and Young People
DAG	Directed acyclic Graph
DIA-X	Diagnostic Expert System for Mental Disorders
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders Fourth Addition

DSM-V	Diagnostic and Statistical Manual of Mental Disorders Fifth Addition
FRI	Family Relationship Index
FTP	File Transfer Protocol
GAD	Generalised Anxiety Disorder
GCT	Germ Cell Tumour
GvHD	Graft versus Host Disease
GSI	Global Severity Index
HADS	Hospital Anxiety and Depression Scale
HES	Hospital Episode Statistics
HL	Hodgkin's Lymphoma
HSCIC	Health and Social Care Information Centre
HSCT	Haematopoietic Stem Cell Transplant
ICCC	International Classification of Childhood Cancer
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th Revision
IES	Impact of Event Scale
IES-R	Impact of Event Scale – Revised version
IES-R-J	Impact of Event Scale – Revised version – Japanese language version
IQR	Interquartile Range
IWS	International Worry Scale
LE	Late Effect
LTHT	Leeds Teaching Hospitals NHS Trust
MHLDDS	Mental Health and Learning Disabilities Dataset
MHMDS	Mental Health Minimum Dataset
MHSDS	Mental Health Services Dataset

MINI	Mini-International Neuropsychiatric Interview
MOS-SSS	Medical Outcomes Study – Social Support Survey
NCRAS	National Cancer Registration and Analysis Service
NCSI	National Cancer Survivor Initiative
NF1	Neurofibromatosis Type 1
NHL	Non-Hodgkin's Lymphoma
OCD	Obsessive Compulsive Disorder
ODD	Oppositional Defiant Disorder
ONS	Office for National Statistics
OR	Odds Ratio
PDS	Post-Traumatic Diagnostic Scale
PTC	Primary Treatment Centre
PTSD	Post-Traumatic Stress Disorder
RAND-36	36 item form developed by the Research And Development Corporation
RB	Retinoblastoma
RCC	Renal Cell Carcinoma
RR	Relative Risk
SCCSS	Swiss Childhood Cancer Survivors Study
SCL-90-R	Symptom Checklist (90 item form) – Revised version
SF-36	Short Form Survey (36 item form)
SI-PTSD	Structured Interview for Post-Traumatic Stress Disorder
SJLife	St Jude Lifetime Cohort Study
SNRI	Selective Noradrenaline Reuptake Inhibitor
SPN	Subsequent Primary Neoplasm
SSRI	Selective Serotonin Reuptake Inhibitor
STS	Soft Tissue Sarcoma

TBI	Total Body Irradiation
TCT	Teenage Cancer Trust
TYA	Teenagers and Young Adults
WHO	World Health Organisation
YSR	Youth Self Report
YSRCCYP	Yorkshire Specialist Register of Cancer in Children and Young People

Chapter 1 Introduction

1.1 Cancer in Children and Young People

1.1.1 What is Cancer?

Cancer is the term given to a group of diseases which are characterised by the uncontrolled proliferation of abnormal cells[1,2].

Cancer can occur in any tissue in the body, and may affect individuals of all ages and backgrounds. However, there are some factors which make the development of cancer more likely. In adult patients, these include lifestyle factors, such as tobacco usage[3], excessive alcohol consumption[4] and obesity[5]. Genetic factors may predispose to cancer in both adults and children. Genetic factors associated with increased risk of cancer include cancer predisposition syndromes such as Li Fraumeni[6] and constitutional mismatch repair deficiency syndrome[7], as well as other disorders where increased risk of malignancy is part of a wider clinical spectrum, such as Trisomy 21 (Down's syndrome)[8], neurofibromatosis type 1 (NF1)[9] and Fanconi anaemia[10].

Approximately 50% of all people are expected to develop cancer during their lifetime[11], and cancer is the cause of more than a quarter of all deaths in the United Kingdom[12], although the majority of these cases and deaths occur in the adult population.

1.1.2 Epidemiology

Childhood cancer (diagnosed under the age of 15 years) is a rare entity, accounting for just 1% of all cancer cases[13]. However, incidence of cancer in children has been steadily rising globally since the late 1970s[14]. Incidence rates of childhood cancer have increased by around a quarter in this period, rising slightly more in girls than boys, although cancer remains more common in boys[14]. Between 2012 and 2014, there were 164 new cancer cases for every million boys and 147 for every million girls in the UK[14]. Figure 1.1a shows the increasing incidence of childhood cancer between 1993 and 2016. Teenage and young adult (TYA) cancer (diagnosed between the ages of 15 and 24 years) has risen markedly in the same time period, with 280 new cancer cases for every million males and 307 for every million females in the UK between

2012 and 2014[15]. Figure 1.1b shows the increasing incidence of TYA cancer between 1993 and 2016.

Figure 1.1a Incidence of childhood cancer per million per year between 1993 and 2016. Image from Cancer Research UK[14]

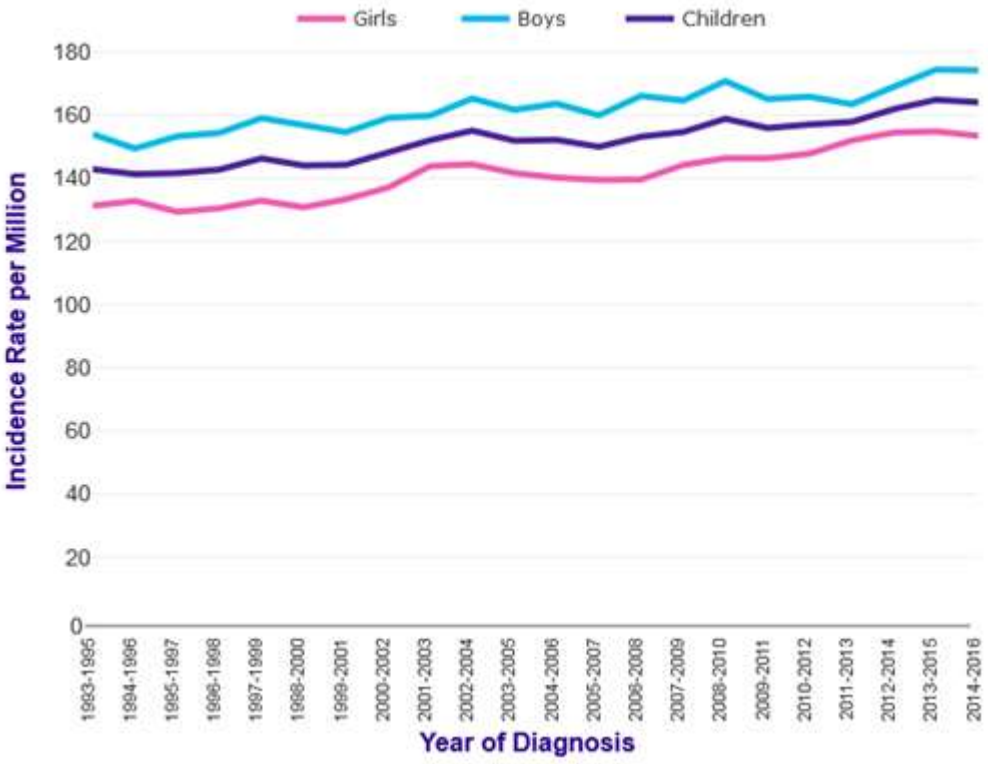

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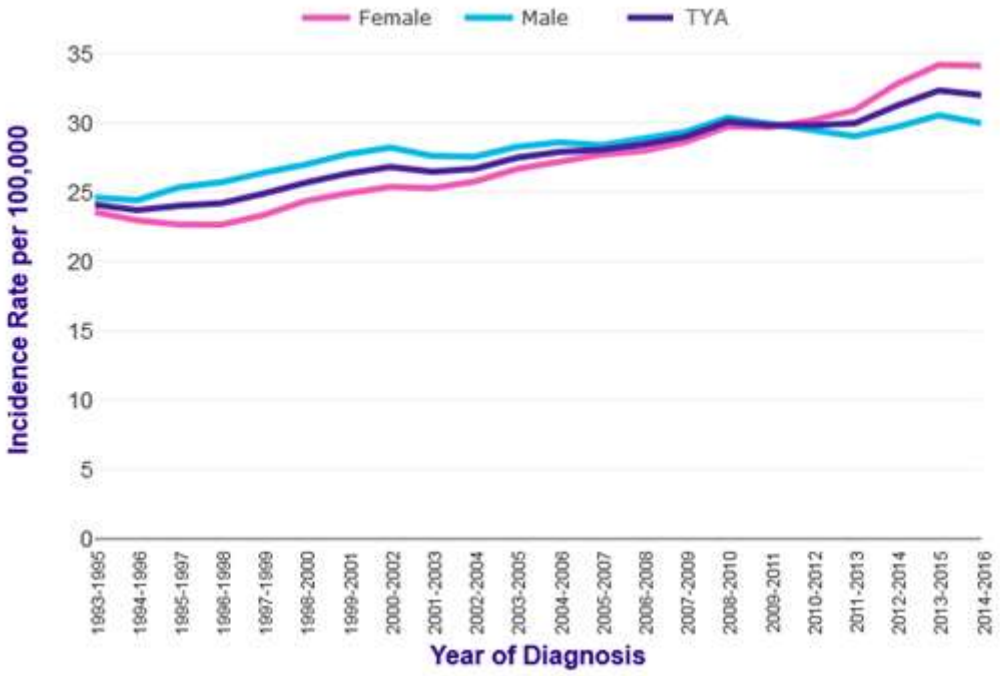
Figure 1.1b Incidence of TYA cancer per 100,000 between 1993 and 2016. Image from Cancer Research UK[15]



Cancers in children and young people (CYP) present an important health issue, not just because of their increasing number but because they may result in considerable mortality. The term “children and young people” in this context refers to children plus TYA, i.e. all cancer patients 24 years of age and younger. Cancer is the leading cause of death in children, accounting for around 20% of deaths in 1 to 14 year olds[16]. Cancer is the leading cause of death in female TYA, and the leading cause of death from disease in male TYA, although transport accidents account for more deaths in this group[17]. Moreover, when cancer affects CYP, there are potentially many more years of life lost than when it affects older adults[18]. As well as being a leading cause of mortality, CYP’s cancer can result in marked morbidity and associated cost[19], with much of this morbidity persisting for the duration of the CYP’s lives[20].

Since the late 1970s, in the same time period that CYP’s cancer rates have increased, survival rates have dramatically improved. The survival rates for childhood cancer have more than doubled[21] and those for TYA have also improved considerably[22]. More than 80% of children and young adults diagnosed with cancer now survive for at least 5 years[21,22] and three quarters of children diagnosed before the age of 15 survive for at least 10 years[21]. Figure 1.2a shows 1, 5 and 10 year survival for children diagnosed with cancer between 1971 and 2010, broken down by cancer type. Although TYA survival rates have not increased as sharply as childhood survival rates, this is offset against an already much higher baseline[22]. Figure 1.2b shows five-year survival estimates for TYA diagnosed with cancer between 1991 and 2005. The prevalence of adult survivors of CYP’s cancer is consequently ever increasing. It has been estimated that there are currently over 35,000 adult survivors of childhood cancer living in Great Britain[23], although this estimate is based on somewhat dated information[24]. As a result, any morbidity burden experienced by this population takes on increasing importance to health and social care economies.

Figure 1.2a 1, 5 and 10 year survival for children diagnosed with different cancer types between 1971 and 2010. Image from Cancer Research UK[21]

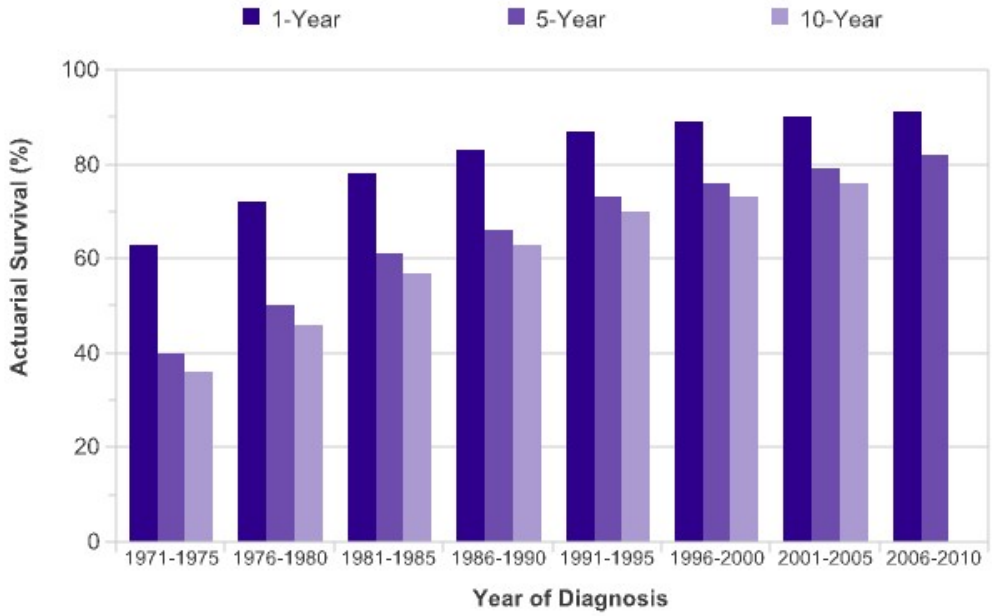
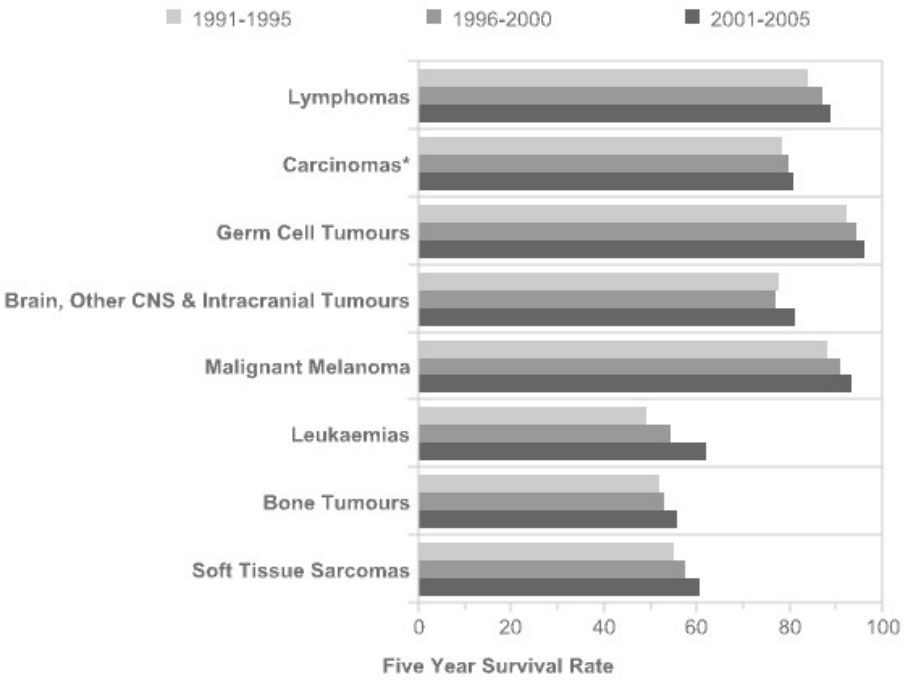


Figure 1.2b 5 year survival rates for TYA diagnosed with cancer between 1991 and 2005. Image from Cancer Research UK[22a]



[a] CNS = central nervous system

1.1.3 Cancer Classification

Cancer in CYPs is biologically distinct from adult cancer, and is therefore classified differently, according to morphological features. Childhood cancer is classified according to the International Classification of Childhood Cancer (ICCC)[25], whilst TYA cancer is usually classified according to the Birch system[26]. The commonest cancers in children (under 15 at diagnosis) in the United Kingdom are leukaemias (approximately 434 new cases per year) and central nervous system (CNS) tumours (approximately 329 new cases per year)[27,28] whilst carcinomas (576 new cases per year) and lymphomas (461 new cases per year) are the most common cancers in TYA[29]. This is in contrast to adults, for whom breast, prostate, lung and bowel cancers are the most common diagnoses[30]. These differences in biology and classification mean that it is essential for CYP's cancer to be studied thoroughly, and separately from cancer affecting older adults. Figures 1.3a and 1.3b show the most common cancer types by age for males and females, respectively.

Figure 1.3a Most common cancer types by age at diagnosis, for male patients. Image from Cancer Research UK[30].

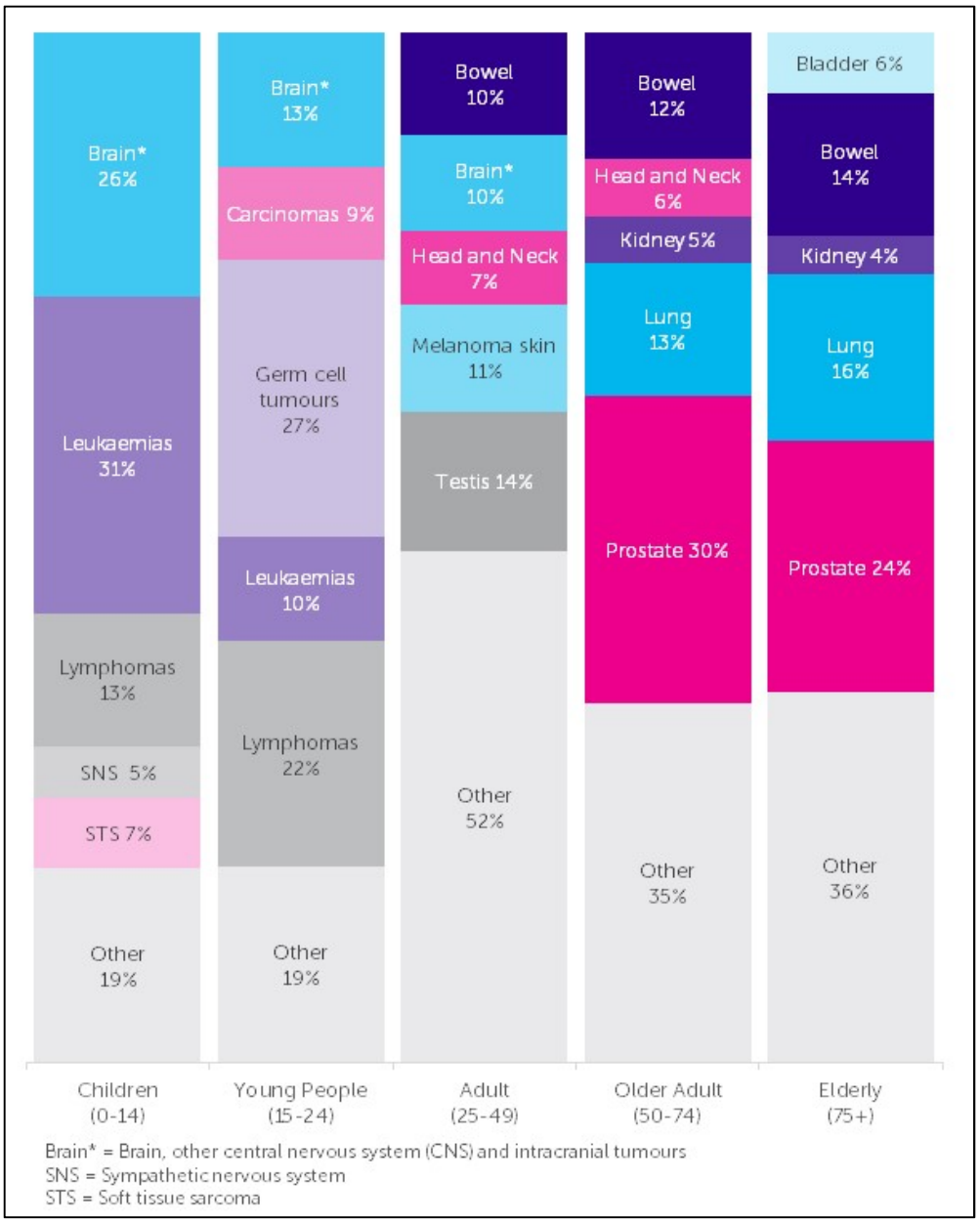
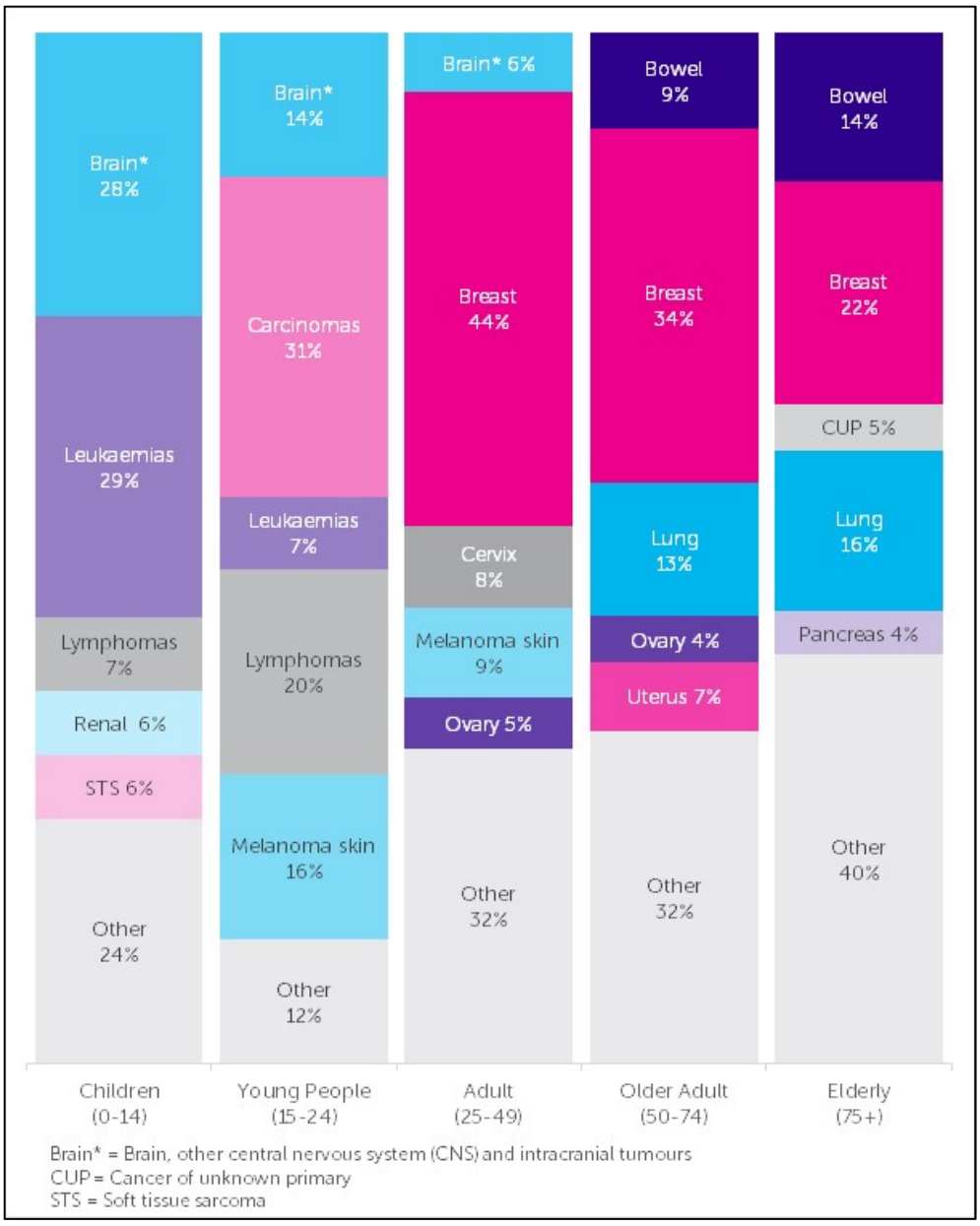


Figure 1.3b Most common cancer types by age at diagnosis, for female patients. Image from Cancer Research UK[30].



1.1.3.1 Leukaemias

The term leukaemia refers to a malignant disease of the haematopoietic tissues[31]. Both the ICCC and Birch systems classify leukaemias as their first major diagnostic group. This group accounts for the greatest number of childhood cancer cases[27], although a smaller number of TYA cancers[15]. As well as being common, leukaemias are survivable, with over 80% of children diagnosed between 2001 and 2005 surviving for at least 5 years[32].

Acute lymphoblastic leukaemia (ALL) is the commonest form of leukaemia, accounting for around 75% of leukaemia cases in children, and around 30% of all childhood cancers[27]. Incidence peaks at 1-4 years of age, at 80-85 cases per million per year[14]. In TYA, ALL accounts for 46% of leukaemias, but only 9% of overall cancers[15]. The prognosis in ALL has improved dramatically over time[33], and the 5 year survival rate for children in the UK is now well over 90%[34]. Although survival is slightly lower in TYA, it is still approaching 80%[35]. Thus, a large proportion of long-term cancer survivors will have had an initial diagnosis of ALL.

Acute myeloid leukaemia (AML) accounts for fewer leukaemia cases in CYP, but still comprises a substantial proportion[36]. Incidence has an early peak in the first year of life, at around 16 cases per million per year, and then falls to 4-7 cases per million per year throughout childhood[14]. Incidence then increases with age, to 10-15 cases per million per year in TYA[37]. The prognosis for AML is less positive than for ALL, with mortality around 40%[38].

Other forms of leukaemia are much less common in the CYP population.

1.1.3.2 Lymphomas

Lymphomas, or malignant diseases of the lymphatic tissues, are considered as a distinct diagnostic group by both the ICCC and Birch systems. Some analyses and definitions will group leukaemias and lymphomas together as “haematological malignancies”[39]. Lymphomas account for a considerable proportion of TYA cancers[29] and, like leukaemias, have a good prognosis, with 5 year survival well above 80%[32].

Hodgkin’s lymphoma (HL) accounts for a large proportion of CYP lymphoma cases, accounting for 45% of cases in children[14] and two-thirds of cases in TYA[15] and has an excellent prognosis, with 5 year survival rates around 98%[35].

HL has an incidence of under 10 per million per year in the under 10s, but this increases rapidly throughout the TYA age group to almost 50 cases per million per year in older TYA[40].

Non-Hodgkin's lymphoma (NHL) has a less favourable prognosis, although survival still exceeds 80%[35]. Incidence is 1-3 cases per million per year throughout the CYP age group[41].

1.1.3.3 Central Nervous System Tumours

CNS tumours are also a distinct group in both the ICCC and Birch systems, and are the commonest solid tumour type in children[27]. Survival from CNS tumours differs markedly amongst different tumour sub-groups. CNS tumours are classified according to the World Health Organisation (WHO) grading system[42]. Grading is from I to IV; grade I tumours are slow growing, non-malignant tumours associated with good long term survival and grade IV tumours are highly aggressive, rapidly growing malignant tumours associated with much poorer outcomes.

CNS tumours affect similar numbers of individuals throughout the CYP age group, with around 50 cases per million per year[43].

For the purposes of this thesis, grade I and II tumours have been grouped together as "low grade" tumours and grade III and IV tumours have been grouped as "high grade" tumours.

1.1.3.4 Neuroblastoma

Neuroblastomata are rare tumours of the primordial neural crest cells, which mainly affect very young children. The incidence of neuroblastoma in the under 5s is 20-25 cases per million per year, but falls sharply thereafter to around 1 per million per year in 10-14s[28]. Neuroblastomata are extremely rare in the TYA age group[44]. The ICCC classifies neuroblastoma as a distinct group, whereas under the Birch system they would be classified within "miscellaneous specified neoplasms". Despite being classified as a single disease, and originating from the same cell type, there are major differences between sub-types of neuroblastoma. Some low-risk sub-types, commonly seen in infants, have an excellent prognosis with minimal or even no treatment, whilst high-risk disease is highly aggressive and has survival rates of less than 50%[44]. Risk stratification is based on factors including age at diagnosis, stage, cytogenetic

factors such as MYC-N amplification status, and histological features[45]. The International Neuroblastoma Risk Group have produced comprehensive guidelines to allow appropriate assessment of risk for individual patients[46]. MYC-N amplification always confers a poorer prognosis and all tumours with this finding are considered high risk. Localised and well differentiated tumours are lower risk than metastatic and poorly differentiated tumours[45].

1.1.3.5 Retinoblastoma

Retinoblastoma is a very rare ocular tumour seen in very young children. Like neuroblastoma, it is classified as a distinct tumour group by the ICCC but would be classified within “miscellaneous specified neoplasms” by the Birch system. There are just over 10 cases per million per year in the under 5s annually in England, and almost no cases in older children or TYA[28]. Although survival is almost 100% in the developed world, retinoblastoma is often associated with constitutional mutations in the RB1 tumour suppressor gene. Individuals with this gene mutation have a 50% risk of a further malignancy by the age of 50[47].

1.1.3.6 Renal Tumours

Using the ICCC, all tumours of the kidneys are classified together. Under the Birch system, renal tumours would fall into varying categories. Renal cell carcinomas (RCCs) would be categorised alongside other carcinomas, whilst Wilms tumours, which are the commonest renal tumour seen in children, are classified within “miscellaneous specified neoplasms”.

Renal tumours have an incidence of 10-20 per million per year for children, but are rare in TYA, with under 10 cases per million per year annually in the UK[48].

Wilms tumours, which account for around 95% of renal tumours in children and about 5% of childhood cancers in total[49], have an excellent prognosis, with survival of over 90%[50]. Although Wilms tumours are rarer in older patients, those aged over 16 with Wilms tumour have a worse prognosis, with 5 year survival being closer to 70%[49].

RCCs are extremely rare in the paediatric population, but become more common in TYA. Survival for both children and TYA is around 60%[51].

1.1.3.7 Hepatic Tumours

Like renal tumours, all tumours affecting the liver are classified into one group by the ICCC. Whilst the Birch system does not have a specific category for hepatic tumours, they are most likely to fall within either carcinomas (e.g. hepatocellular carcinoma) or “miscellaneous specified neoplasms” (e.g. hepatoblastoma).

Liver tumours in childhood are rare, and only account for around 1% of paediatric cancers. Hepatoblastoma, the most common childhood liver tumour, is associated with a good prognosis and 5 year survival over 80%, although many patients require liver transplantation if the tumour cannot be surgically resected. Transplantation has considerable associated long-term morbidity[52]. Throughout the CYP age range, hepatic cancers have an incidence of fewer than 10 cases per million per year[53]. Liver cancers are extremely rare in the TYA population[53].

1.1.3.8 Bone Tumours

Both the ICCC and Birch systems classify malignant bone tumours as distinct groups. Bone tumours account for 3-5% of cancers in children and 7-8% of cancers in TYA[54]. The commonest bone tumours in CYP are osteosarcoma and Ewing’s sarcoma. Survival from bone tumours is lower than many other cancer types, at just under 60% for children and just under 50% for adolescents[54]. Bone tumours have an incidence of 5-12 cases per million per year in children, but up to 190 cases per million per year in males aged 15-19[55].

1.1.3.9 Soft Tissue Sarcomas

Like bone tumours, soft tissue sarcomas (STSs) are classified as a distinct group by both the ICCC and Birch systems. STSs account for around 7% of paediatric cancers[56]. STSs have an incidence rate of 10-13 cases per million per year in the under 5s, this rate then falls in older children[28] and then increases in TYA to just over 20 cases per million per year in older TYA[57]. Survival from STSs is between 75 and 80% across the CYP period[58].

1.1.3.10 Germ Cell Tumours

Germ cell tumours (GCTs) are another distinct group in both the ICCC and Birch classification systems. In the paediatric population, GCTs are relatively

rare, comprising around 3% of cancers[59], with incidence rates between 1 and 7 cases per million per year[28]. In TYA, however, GCTs are amongst the more common cancer types, with an incidence around 35 per million per year[29]. Males are disproportionately affected, mostly due to the prevalence of testicular GCTs, which are the commonest cancers in young men. Prognosis is extremely good, with 20 year survival at 90%[59].

1.1.3.11 Skin Cancers

Whilst skin cancers are categorised with “other malignant epithelial neoplasms and malignant melanomas” in the ICCC, they are a distinct category in the Birch system. Skin cancers are very rarely seen in children, but incidence increases steadily after the age of 20[60], with rates of 35-40 per million per year in TYA[29]. Prognosis is excellent, with 30 year survival amongst CYPs at 93%[61].

1.1.3.12 Carcinomas

Carcinomas are cancers arising from epithelial tissues. The Birch system has a distinct category for carcinomas, whilst in the ICCC they are largely categorised with “other malignant epithelial neoplasms and malignant melanomas”, although depending on their anatomical location, they may also fall within other categories, such as renal or hepatic tumours. They are rare tumours in the paediatric population, but are the commonest tumour type in the TYA age group[29]. Incidence of carcinoma in the TYA group is increasing year on year, and now exceeds 50 cases per million per year[29]. Much of this increase has been due to increasing rates of thyroid carcinomas, as well as smaller increases in rates of both cervical and ovarian carcinomas[29]. The reasons for the increase in thyroid cancer rates are unclear, although this trend has been noted globally[62]. There has been some suspicion that the increased rate is due to over diagnosis of small, indolent tumours which are unlikely to cause much morbidity, however it has also been noted that larger, more aggressive tumours have become more common, meaning that any increase cannot be explained solely by over diagnosis[63].

Survival from carcinomas is varied and depends upon factors such as anatomical location and disease stage. Thyroid carcinoma has a very good prognosis, with around 98% of affected individuals surviving for 5 years or more, whereas 5 year survival for bowel carcinoma is much lower, at around

65%[15]. In females in this age group, cervical, breast and ovarian carcinomas are not uncommon. 5 year survival is around 80% for breast and cervical carcinomas, and around 85% for ovarian carcinomas[15]. Amongst patients with breast cancers, survival is directly proportional to stage at diagnosis, with metastatic disease having a much poorer prognosis than localised, low stage disease[64], and similar patterns are seen in colon cancer[65].

1.2 Cancer Registration

Cancer registration is defined as "the systematic collection of data about cancer and tumour diseases"[66]. Cancer registration is an important way of gathering epidemiological data about cancer, and may help to identify groups who seem to be disproportionately affected by cancer and who would benefit from public health interventions such as screening programmes. Additionally, ongoing follow up of individuals with records on such registries may allow the study of the long-term health of affected individuals once they have recovered from their primary disease.

1.2.1 The Yorkshire Specialist Registry of Cancer in Children and Young People

The Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP), which forms one of the main data sources for this thesis, has collected population-based data on cancer diagnoses in children within Yorkshire for over 40 years[67]. The history of, and methodology used by, the YSRCCYP are further described in Chapter 3: Data Sources and Methods.

1.3 Childhood and Young Adult Cancer Treatment Centres

1.3.1 Principal treatment centres for Children

All children aged 17 and under with cancer who are treated in Great Britain will have their care co-ordinated by one of 19 paediatric principal treatment centres (PTCs)[68]. These are hospitals with specialist knowledge and experience of caring for these young patients. The co-ordination of care by these specialised centres developed in response to national guidance aiming to improve outcomes in children with cancer[69], and there is evidence that specialist centres who treat a higher volume of patients do have better outcomes[70].

Within Yorkshire, the two PTCs are Leeds Children's Hospital and Sheffield Children's Hospital.

1.3.2 Principal treatment centres for Teenagers and Young Adults

Young people have distinct needs when accessing healthcare. The government produces a set of "Quality criteria for young people friendly health services", known colloquially as the "You're Welcome" criteria, which set out principles for ensuring healthcare services meet the needs of teenagers and young people. The most relevant of these to the provision of cancer care are those falling under the "Environment" theme, which recommend that care is delivered in a safe, suitable, young-people friendly environment[71]. Additional recommendations include all staff members who deliver care to young people having suitable training in caring for this age group, services being accessible to all young people, and young people being routinely involved in the evaluation of services they access.

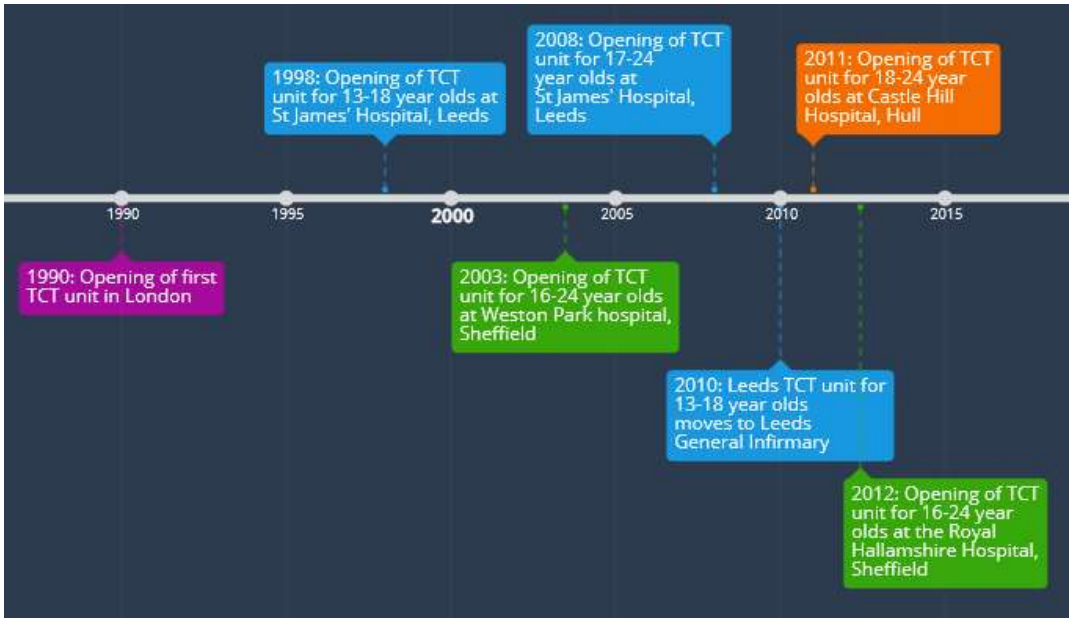
In Britain, teenagers and young people aged 18 and over have the option of having their care co-ordinated by one of 15 PTCs specialising in young people's care, or by having all of their care at a non-specialist oncology centre closer to their home[69]. Many young people in England receive the majority of care out-with one of these PTCs[72]. Both Leeds Teaching Hospitals NHS Trust and Sheffield Teaching Hospitals NHS Trust are PTCs for young adults[73].

1.3.3 Specialist Teenage and Young Adult Units

The Teenage Cancer Trust (TCT) are a charitable organisation who specifically aim to improve the care and experiences for young people being treated for cancer between the ages of 13 and 24[74]. They fund specialist wards caring for patients within this age group, within hospitals which may or may not be designated PTCs. Within Yorkshire, there are five units at different locations; Castle Hill Hospital in Hull (for 18-24 year olds), Leeds Children's Hospital (13-18 year olds), Royal Hallamshire Hospital in Sheffield (16-24 year olds), St James' University Hospital in Leeds (17-24 year olds) and Weston Park Hospital in Sheffield (16-24 year olds), which have opened between 1998 and 2012, as shown in figure 1.4[75]. In practice, these units provide a similar service, whether or not they are designated as PTCs, providing age-specific care, access to youth support workers and recreational facilities such as Wi-Fi and

games consoles[75].There is some overlap between the age ranges catered for in these units, and whether a 17 year old patient is treated in a centre aimed more at young teenagers aged 13-17 or 18 or at young adults aged 17-24 is a complex decision made by a multi-disciplinary team, taking into account both clinical factors such as underlying diagnosis and social factors such as whether a young person is still in full time education and living with their parents[69].

Figure 1.4 Dates of opening of specialist TCT treatment centres across Yorkshire



1.4 Treatment of Childhood and Young Adult Cancer

Cancer treatment is constantly evolving as research is undertaken and more is learned about tumour biology and potential new therapeutic targets. The majority of cancer treatment, however, consists of therapies which fall into three broad categories; surgery, chemotherapy and radiotherapy. Newer therapies, such as immunotherapy and targeted antibody treatments, are also being developed and becoming a more standard part of some treatment regimes.

1.4.1 Surgery

Surgery to remove all or part of a tumour may be the only treatment required for a cancer or brain tumour, or it may be used in conjunction with chemotherapy and/or radiotherapy. Although more targeted than systemic drug

therapy, surgery is not without risk of long-term complications. Abdominal surgery, particularly on large masses presenting early in life, may result in difficulties with bladder and bowel function, including incontinence[76]. Surgery for brain tumours, even in the absence of other therapies, may result in neurocognitive difficulties, neurological deficit or visual impairment[77].

1.4.2 Chemotherapy

Chemotherapy refers to the use of cytotoxic agents to treat cancer. Chemotherapy may be used as a sole treatment modality or in combination with radiotherapy, or may be used to shrink a tumour in order to make it more amenable to surgery or to treat residual tumour which cannot be surgically resected. Traditionally, chemotherapy is given systemically. This means that, as well as treating cancer cells, it also impacts on the bodies' normal tissues. This results in side effects and potential long-term consequences[78]. Chemotherapy generally acts by inhibiting cell division, exploiting the fact that cancer cells often divide much more rapidly than healthy cells. Healthy cells which do divide rapidly, such as hair follicles and gastric mucosa, are at the greatest risk of damage from chemotherapy[78].

Over time, increased understanding of the long-term impact of chemotherapy, combined with greater knowledge of which cancers can successfully be treated with less intensive treatment, has led to some conditions being treated successfully with less intensive chemotherapy regimens[79,80].

Conversely, some conditions which were previously considered to have a very poor prognosis are now treated with more intensive treatments. Survival rates for high-risk neuroblastoma, for example, have improved considerably over time, partly due to the use of more intensive chemotherapy regimens[81].

1.4.3 Radiotherapy

Radiotherapy is the use of targeted radiation to treat cancer. It is rarely used as a sole curative treatment modality, but is often used to treat residual tumour which cannot be surgically resected or as part of a combined regimen alongside chemotherapy. Although total body irradiation (TBI) is now rarely used (an exception being prior to haematopoietic stem cell transplant) and most radiotherapy is targeted, the radiation beam will always pass through some normal tissues. This can lead to severe side effects and damage which

may be long lasting. Factors including age at time of therapy and dose of radiotherapy affect the likelihood of side effects developing[82]. Skin changes are seen very frequently following radiotherapy, and can have a serious negative impact on quality of life[83]. Other side effects of radiotherapy include diarrhoea, nausea and fatigue[84]. Syndromes associated with DNA-repair defects are associated with considerable late effects from radiotherapy, particularly SPNs[85].

Like chemotherapy, there have been temporal changes in the way radiotherapy is used. Radiotherapy is used far less frequently in Wilms tumours and localised neuroblastoma[80], and at reduced intensity for patients with HL[86]. Prophylactic cranial radiotherapy, which was once a routine part of treatment, is no longer used in ALL[79].

TBI continues to be used for conditioning prior to stem cell transplant, but concerns regarding considerable toxicity in both the long and short term[87] have led to the development of lower-dose TBI regimens[88,89].

1.4.4 Immunotherapy

Immunotherapy, which is the use of antibody treatments to target cancer cells, has been developed for childhood cancers such as neuroblastoma over the past 2 decades[90]. This has been pioneered in an attempt to produce treatment which is more targeted and less likely to damage healthy tissues and cause long-term compilations. Unfortunately, many of these compounds are highly immunogenic and therefore associated with risk of hypersensitivity and anaphylactic reactions. Acute toxicities range from headaches and myalgia to cytokine storm, which can be potentially fatal[91]. Due to their relatively recent development, less is known about potential long-term complications than more established therapies such as chemotherapy and radiotherapy. It is hoped that these treatments will be associated with fewer long-term complications than other therapies[91].

1.5 Late Effects of Childhood and Young Adult Cancer

Although most CYP with cancer will survive[21,22], this is not without complications or consequences. The non-specific and highly toxic nature of many cancer treatments means that the majority of children and young people

who survive cancer will go on to develop treatment-related complications, some of which may occur many years after treatment has ended[92]. One large British study found that adults who had survived childhood cancer had 11 times the expected mortality rate in the 20 years post diagnosis, and mortality rate remained elevated above that of the general population 45 years post diagnosis[93]. Over two thirds of survivors will have at least one chronic health condition 25 years after diagnosis[94] and 80% have at least one serious chronic disease by the age of 45[95] with some estimates even higher[96]. The majority self-report decreased quality of life, which has been directly attributed to these ongoing health problems; these reports come from patient-reported outcome measures such as the SF-36, which include reports on domains including pain, social functioning and mental health[97].

1.5.1 Risk of Late Effects

Whilst the majority of long-term CYP's cancer survivors are at risk of late effects (LEs), some are at a much higher risk and some are at minimal risk. A strategy for stratifying patients, and thus adapting their planned follow-up, based on risk of LEs was first proposed by Wallace *et al* in 2001[98]. These levels of risk are based largely on the intensity of cancer treatment given, with those who have received minimal systemic treatment who are therefore at minimal risk of LEs being classified as level 1 and those who have received intensive therapies who are at the highest risk of LEs being classified as level 3. The majority of patients will be classified as level 2 and be at moderate risk of LEs. Despite the relatively crude and simplistic nature of this classification system, it has been shown to accurately predict risks of physical ill health such as cardiac and renal failure in a large cohort of British CYP's cancer survivors[99]. Further work by the National Cancer Survivor Initiative (NCSI)[100] has led to the development of guidelines on long-term follow up of CYP's cancer survivors, based upon late effects risk, which have been adapted around the world[101].

1.5.2 Late Effects over Time

As cancer treatments have become more targeted and treatment regimens have reduced in intensity where possible, it stands to reason that patients treated more recently should be at risk of fewer late effects than those treated longer ago. This has been demonstrated in a very large cohort study from the

United States, which found decreased risks of late morbidity in patients diagnosed and treated more recently compared with those treated longer ago[102]. However, survival rates of cancer are increasing, and some patients who may previously have died are now surviving, albeit with long-term morbidity. In some cases, survival is a result of more intensive therapy for diseases which would once have had extremely poor prognoses. Thus in one large cohort of leukaemia patients, there was no decrease in late effects in patients treated more recently compared to those treated longer ago[103]. It may be that the difference in late morbidity amongst leukaemia patients compared to those treated for other malignancies may relate to patients who are now surviving conditions which previously would have been fatal, and that the reduction in late effects for patients with lower- risk disease who have received less intensive treatment is somewhat ameliorated in large-scale studies by the prevalence of late effects in patients who received very intensive therapy but who would not previously have survived[104].

1.6 Physical Late Effects

LEs of cancer vary widely, depending upon factors such as the type and dose of treatment used and the age the patient is when undergoing treatment. Survivors of TYA cancer are at greater risk of cardiovascular disease, second malignancy and pulmonary complications, as well as psychosocial difficulties, than survivors of childhood cancer[105].

Many LEs have been known about for many years and the majority are well documented. A number of longitudinal studies, such as the British Childhood Cancer Survivor Study (BCCSS)[106], the Childhood Cancer Survivor Study (CCSS)[107] and the St Jude Lifetime Cohort Study (SJLife)[108] in the USA and the Swiss Childhood Cancer Survivor Study (SCCSS)[109] have followed up patients for several decades and collated data from self-reports and questionnaires on the health problems survivors have developed. Due to their reliance on questionnaires and self-reporting, however, they are all at risk of potential bias as they will not capture data on non-responders. The Adult Life after Childhood Cancer in Scandinavia (ALiCCS) study[110] is a retrospective cohort study which is aiming to gather data from hospitals and disease registries on late effects of CYP's cancer on a population level, which should

enhance the quality of data available on late effects. This study should potentially have fewer issues with bias because data is from registries and hospitals, rather than relying on participants returning questionnaires.

Known LEs include cardiovascular disease[111], reproductive health problems[112] and subsequent primary neoplasms (SPNs)[113]. Respiratory[104], renal[114], endocrine[115] and neurological[116] complications have also been described in the literature. LEs vary depending on the treatment received; for example patients who received chest radiotherapy are at considerable increased risk of developing breast cancer[117], whilst patients treated with anthracyclines may go on to develop cardiomyopathy[118]. Age at diagnosis and treatment of cancer also plays a role in the types of LEs which may develop.

1.6.1 Cardiovascular disease

Diseases of the cardiovascular system are 4-6 times more prevalent in CYP's cancer survivors than the general population[119,120]. This includes conditions such as peripheral vascular disease, valvular heart disease, cardiac failure and myocardial infarction. Stroke risk is also elevated in CYP's cancer survivors[121], with a small but non-negligible subset experiencing recurrent stroke[122]. Survivors of both Hodgkin's and non-Hodgkin's lymphoma are at particular risk of cardiovascular diseases[123], as are patients who have received thoracic radiotherapy or high dose anthracyclines[124].

1.6.2 Subsequent primary neoplasms

Subsequent primary neoplasms are tumours which arise in differing locations, or are histologically distinct, from the initial cancer and are thus distinct from relapse[113] and are a considerable source of anxiety for cancer survivors and their families[125]. Around 1 in 25 CYP's cancer survivors will develop an SPN in the 25 years following their original diagnosis[126]. Survivors of childhood cancer are 3-6 times more likely to develop SPNs than older patients[127], and survivors of TYA cancer are also at increased risk of SPNs compared to older adults[128]. Survivors of TYA cancer often develop an SPN relatively soon after their initial cancer treatment, and shorter intervals between cancer diagnoses are associated with poorer prognosis[129]. SPNs have been observed following treatment for a variety of cancers, including Burkitt's lymphoma[130], retinoblastoma[131], thyroid cancer[132] and malignant astrocytoma[133].

1.6.3 Sexual and reproductive health

Many chemotherapeutic agents, as well as radiotherapy to the lower abdomen and pelvis, may result in sub fertility[112]. Surgery may also result in difficulties achieving or carrying a pregnancy, either due to direct removal of the female reproductive organs[134] or as a result of cervical incompetence following more targeted surgeries[135]. Sexual health problems such as erectile dysfunction[136,137] and decreased arousal[138] are also seen commonly, and are particularly prevalent in those treated for cancer in the TYA period[139]. Difficulties with sexual health[140,141] and sub fertility[142,143] have a considerable negative impact on mental health and quality of life. Conversely, psychological difficulties are one potential cause of sexual dysfunction[144]. Although there are strategies available to try to mitigate sub fertility, there are also multiple potential complications which may occur even if a pregnancy can be successfully achieved[145].

1.6.4 Respiratory disease

Diseases of the respiratory system affect CYP's cancer survivors at a greater rate than the general population, with one in five having at least one respiratory diagnosis by 35 years post diagnosis[146]. Chest radiotherapy is strongly associated with pulmonary fibrosis, with a cumulative incidence of 3.5% by 20 years after the original cancer diagnosis[104]. Cranio-spinal irradiation, which is likely to involve at least some radiation to the chest by virtue of the location of the spine, is also associated with increased risk of respiratory pathology[147]. Chemotherapy with bleomycin is also associated with lung fibrosis, which can be particularly problematic following exposure to high concentration oxygen and thus cause serious potential problems during future general anaesthesia[148].

1.6.5 Renal disease

Many chemotherapeutic agents are nephrotoxic and can cause both acute and late decreases in renal function, particularly platinum compounds, alkylating agents and methotrexate[114]. Reported prevalence of renal dysfunction among long term CYP's cancer survivors varies considerably, but some studies report rates of up to 84%, with nephrectomy and radiotherapy to the kidney being notable risk factors along with the aforementioned chemotherapeutic agents[149].

1.6.6 Endocrine disease

Endocrine disorders are prevalent in CYP survivors, with one study reporting that nearly half had at least one endocrine problem. The greatest risk is seen in those treated for CNS tumours, who are at risk of pituitary damage as a result of surgery or radiotherapy, and Hodgkin's lymphoma[150]. High rates of obesity and metabolic syndrome amongst CYP's cancer survivors, which are risk factors for the development of diabetes mellitus, may explain some of this pathology[151]. Patients exposed to total body irradiation, chest or abdominal radiotherapy, as well as high dose therapy and stem-cell transplants, are at particular risk for developing metabolic syndrome[152,153].

1.6.7 Neurological disease

Aside from stroke, which has already been described in the cardiovascular disease section, neurological disease is not a major LE for many CYP's cancer survivors. However, for survivors of CNS tumours, it can be a major issue. Seizures, motor impairment and sensorineural hearing loss will affect 41%, 35% and 23% of survivors respectively by 30 years post tumour diagnosis[116].

1.7 Late Effects on Mental Health

Despite the obvious emotional impact of a cancer diagnosis[154], relatively little is known about the late effects of childhood cancer on mental health. Both psychological distress[155] and psychiatric disorder[156] have been investigated in long-term survivors of CYP's cancer. Broadly speaking, for the remainder of this thesis, the term "psychological" will be used to refer to any difficulties with emotion or behaviour, whilst "psychiatric" refers specifically to clinical diagnoses. The terms "mental ill health" and "mental health problems" encompass both psychological and psychiatric issues.

There is evidence that childhood cancer survivors are at increased risk of psychological distress in adult life[155], with risk particularly high in those with chronic physical health needs[157]. However, these data come from self-reports and questionnaires rather than clinician-made diagnoses. Self-reporting of symptoms is known to have a low predictive value for psychiatric diagnoses such as depression[158] and even well validated scores are less accurate in the presence of co-morbidity[159]. Patients who report higher levels of psychological

distress are also more likely to utilise mental health services, but again this is based on self-report and not medical records[160]. There are also data from parental reports to suggest adolescents who are survivors of childhood cancer have more behavioural, social and emotional issues than their unaffected siblings[161].

A large Danish study found that there was an increased likelihood of secondary care contact for psychiatric disorders in survivors of childhood, adolescent and young adult cancer compared with sibling controls[162], with the highest risk being in those who were diagnosed under the age of 10. However, as the majority of healthcare contact for patients with psychiatric disorders occurs in primary care[163], it is likely that looking only at hospital contacts will not reveal the true extent of these issues, although they probably provide a good estimate of the prevalence of the most severe mental health problems.

Reports of psychological distress[155,161] come from studies using sibling controls. Whilst siblings provide an obvious control group due to their shared genetics and upbringings, using siblings of cancer survivors in controls when investigating mental health issues is problematic. A diagnosis of any serious childhood illness impacts the whole family, and siblings of CYP diagnosed with cancer face a variety of challenges of their own[164]. Using them as a control group, therefore, is likely to underestimate the effects cancer has on the diagnosed individual. A lack of population-based studies, however, means that at present there are no better data available.

It is known that survivors of childhood cancer are more likely to be prescribed antidepressants than the general population[156,165]. However, in the United Kingdom, first line therapy for mild to moderate depression is psychological therapy such as cognitive behavioural therapy[166]. It is therefore likely that looking at antidepressant prescribing alone will underestimate the prevalence of depression.

Additionally, studies reporting increased antidepressant prescriptions[156,165] have looked purely at prescribing data and did not provide information on the indication for prescription. Various antidepressants, including tricyclics and selective serotonin reuptake inhibitors (SSRIs), have been used to treat neuropathic pain[167]. Pain is another commonly reported symptom in cancer

survivors[168] and therefore without data on indication for prescriptions of antidepressant medication, it is difficult to know how much increased prescribing is actually a result of increased prevalence of depression. One study[156]**Error! Bookmark not defined.** did exclude prescriptions of tricyclic and selective noradrenaline reuptake inhibitors (SNRIs) in a bid to account for this, as these are the drug types most likely to be prescribed for pain, but this would not exclude all prescribing for this indication and data on actual diagnoses would still be valuable. Antidepressant medications, in particular SSRIs, are also used for a number of psychiatric conditions, such as obsessive-compulsive disorder (OCD)[169], generalised anxiety disorder (GAD)[170] and eating disorders[171]. Whilst increased prescribing does likely indicate higher rates of psychiatric illness in this cohort, it would be useful to know specifically which conditions were more prevalent.

Substance misuse has been shown to be lower in survivors of CYP's cancer than the general population[172], presumably as a result of health promotion aimed at reducing LEs. However, data from the referenced study came from a cohort of largely Hispanic patients, and thus may not reflect patterns in the UK. This study also found that depression was associated with an increased risk of marijuana use. The CCSS found lower rates of tobacco smoking and risky alcohol use in survivors of CYP's cancer compared to their siblings[173]. Another American study found similar rates of risky behaviours, including illicit drug use, between cancer survivors and their siblings[174]. As already discussed, the use of siblings as a control group is not without problems and it is thus difficult to interpret these results.

1.8 Link between Physical and Mental Ill Health

Mental health problems are associated with an increased risk of premature mortality, even after adjustment for pre-existing physical conditions[175,176]. Although some mortality is a result of suicide, drug- or alcohol-related causes[177,178], there is also evidence of increased mortality from causes such as cardiovascular[179,180], gastrointestinal, infectious[181]. and metabolic disease[182,183]. This is thought largely to be due to high prevalence of unhealthy lifestyle choices in this group[184], although lack of concordance with medical advice in patients with poorer mental health may also play a role.

Riskier lifestyle choices in patients with mental health problems have also been demonstrated in survivors of CYP's cancer; for example higher rates of marijuana use in survivors with depression[172].

Given the already increased risk of cardiovascular disease in CYP survivors[93,111,118], as well as risk of other diseases which are affected by lifestyle such as SPNs[113,117] and respiratory problems[104], maintaining a healthy lifestyle is particularly important[151], although not always adhered to[185].

It is therefore particularly important that psychiatric morbidity is identified in survivors, not only because it results in considerable distress and reduced quality of life[155,160,161], but also because serious mental health issues may indirectly increase risk of other LEs.

1.9 Young People's Mental Health

Improving the nation's mental health is a key target for the UK government, with many indicators in the Public Health Outcomes Framework relating to mental health[186]. According to data from the Office for National Statistics, as many as 8.2% of adults had self-reported a mental health problem in 2017[187]. Although these data do not report on children under the age of 16, or include any breakdown by age, it does give some indication of the scale of the problem of mental ill health in the UK population. Another large scale survey in working-age adults (16-64 years), which collected data on symptoms as well as diagnoses, estimates the prevalence to be much higher, at 17%[188].
Mental health problems in CYP are especially concerning, because there is evidence that mental health problems in early life are an important risk factor for poor mental health in adulthood, as well as poor educational and socioeconomic outcomes[189–192]. Additionally, mental health problems are strongly associated with premature mortality[175]. Approximately 50% of adult mental health disorders are thought to have their onset by the age of 14 years and approximately 75% by 24 years[193,194], with some studies finding large numbers beginning even earlier, reporting onset of up to three quarters of adult mental health issues before the age of 18[195]. A large British cohort study also reports a 1.5 to 2 fold increase in mental health difficulties in later life in those individuals who had psychological difficulties in childhood and early adulthood[196]. It is estimated that fewer than half of young people with a mental

health problem receive appropriate therapy, which may explain why many of these disorders persist into later life[197,198].

Globally, mental health problems affect around 13.4% of children and adolescents; depression affects around 2.6% and anxiety affects around 6.5%[199]. In the UK, approximately one fifth of young people develop mental health problems during adolescence[177]. In the latter quarter of the last century, there was also a considerable increase in suicides, particularly in older male teenagers [197].

Risk factors for poor mental health in early life include bullying[200], poor parental mental health[201,202] , deprivation[203] and low cognitive ability[204]. Poor diet quality has also been associated with risk of poor mental health amongst children and young people[205], which may reflect the link between deprivation and diet. Being female is also a risk factor for mental health problems at any age, with some evidence that females are more likely to be adversely affected by triggers such as educational[206] and financial stressors[207]. Early cessation of formal education and low attainment is both a risk factor for, and consequence of, poor adolescent mental health[208]. Students who were disengaged with education were more likely to have psychological problems, but directionality has not been clearly established[209]. As well as being associated with increased likelihood of developing mental health problems[202], deprivation has also been linked to decreased rates of referral to specialist mental health care following episodes of self-harm[177].

1.9.1 Mental Health of Young People with Chronic Illness

CYP with chronic physical health conditions are known to be at markedly increased risk of developing mental health problems compared to their physically healthy counterparts [210,211], and conversely, young people with mental health problems are at increased risk of physical health problems[212]. Adjusting to a chronic disease, particularly in adolescence, is challenging and physical health problems in young people are a strong predictor of future mental health service use[212]. Even in the absence of diagnosed psychiatric illness, physical illness is a risk factor for suicide[213].

There are a number of factors which may explain the increased risk of mental ill health in CYP with chronic illness. The diagnosis of a chronic illness in a child

or young adult is often a shock to the whole family and requires a period of adjustment for both the affected young person and their caregivers[214]. CYP who struggle to adapt to the diagnosis of a chronic illness are at particular risk of mental health problems[215]. Patients with pre-existing alexithymia, who struggle to identify and express their emotions, are more likely to develop maladaptive coping strategies and also go on to experience worse mental health[216]. CYP whose parents struggle to adapt to their diagnosis and suffer from their own mental health problems as a result have worse health-related quality of life and more mental ill health than CYP whose parents cope well with the diagnosis and maintain good mental health[217]. This likely reflects the known link between poor parental mental health and risk of developing psychiatric illness in adolescence[202].

Like other chronic illnesses, a diagnosis of cancer can be hugely emotionally challenging[154] and it stands to reason that similar challenges to those faced by CYP with other diagnoses are also applicable to CYP with cancer.

Feelings of shame, unattractiveness and embarrassment are associated with some chronic illnesses, particularly those which lead to changes in physical appearance[218]. Treatment for cancer can lead to marked physical alterations, most obviously alopecia secondary to chemotherapy, but also potentially more permanent changes such as amputation, enucleation and surgical scarring. Radiotherapy can also result in skin and hair changes, with patients who have undergone cranial radiotherapy at risk of long-lasting hair thinning, which may be distressing[219]. Poor growth and subsequent short stature may develop as a result of prolonged illness as well as cancer treatments[220–222]. These physical changes are likely to lead to the same feelings of shame, unattractiveness and embarrassment encountered by young people with other conditions.

Feelings of belongingness and “fitting in” at school are associated with better mental health, but young people with disabilities and ill health are less likely to feel a sense of belongingness than their physically healthy peers[223]. Bullying has a considerable negative impact on mental health[200] and social exclusion has a stronger association with mental illness than other forms of bullying[224]. Bullying is also associated with more frequent relapse of mental health problems[225]. Bullying is known to be a major problem for young people with a

cancer diagnosis[226], and it is likely that this has a major negative impact on subsequent mental health.

Children with chronic illnesses may be bullied and feel different from their peers as a result of their health problems[227,228] and experience greater feelings of loneliness and isolation during their school life[229]. Children with chronic ill health are also more likely to be victims of multiple forms of bullying[230]. Expectation of judgement and bullying from peers may also prevent CYPs from sharing their diagnosis with their peers and thus deprive them of potential support[231]. Additionally, many caregivers are more protective of chronically ill CYP than they would be of their healthy siblings, leading to a reduction in opportunities to gain independence and spend time socialising with their peers[232].

CYP who have experienced a cancer diagnosis may go on to have considerable difficulties with romantic attachments[233]. These may be in part due to the aforementioned physical changes, which result in feelings of shame and unattractiveness[218]. Anxieties regarding sub-fertility and sexual function[139,234], as well as reduced libido and interest in dating[235] may impact on the development of romantic relationships. Anxieties regarding when to disclose their history of cancer, and how this information will be received by a potential romantic partner, are also potentially problematic[233]. Absence of romantic relationships is strongly associated with poorer mental health[236].

1.9.2 Classification of Mental Illness

Within most UK hospitals, the diagnosis and classification of mental illnesses is based on the International Statistical Classification of Diseases and Related Health Problems 10th Revision (known more commonly as the ICD-10)[237]. This differs to the USA, where the Diagnostic and Statistical Manual of Mental Disorders Fifth Addition (known as DSM-V) is used[238].

The ICD-10 classifies illnesses, including mental illnesses, by affected bodily system and then disease pattern. All mental illnesses have the prefix “F”.

1.9.2.1 F00-F09 Organic, including symptomatic, mental disorders

These are conditions characterised by a clear organic aetiology, and comprise largely of dementias and cognitive difficulties[237]. These disorders are not

considered within this thesis, as the cognitive late effects of CYP's cancer have been comparatively well studied already[239–241].

1.9.2.2 F10-F19 Mental and behavioural disorders due to psychoactive substance use

These conditions are those which occur as a result of substance use and misuse, including dependency and withdrawal of substances[237]. These conditions are of interest, at least in part due to their considerable impact on physical health[174].

1.9.2.3 F20-F29 Schizophrenia, schizotypal and delusional disorders

These disorders are characterised by periods of psychosis[237], a debilitating symptom where the patient suffers hallucinations and/or delusions without insight and has an impaired understanding of reality[242]. Whilst comparatively rare, with a prevalence around 1%, these disorders are important due to the marked functional impairment they can cause[243].

1.9.2.4 F30-F39 Mood [affective] disorders

These disorders are primarily characterised by a change in affect, and include mania and depression[237]. Affective disorders in adolescence are associated with poor health outcomes in later life[175] and are thus of interest amongst cancer survivors who are already at risk of long-term poor health[108]. Affective disorders are also the most common mental health conditions in the UK[188].

1.9.2.5 F40-F48 Neurotic, stress-related and somatoform disorders

These disorders are characterised by stress and anxiety, either generally or in specific situations or in response to specific events; post-traumatic stress disorder (PTSD) is included within this classification[237]. These are also common within the UK[188], and are likely to be common amongst cancer survivors[244,245].

1.9.2.6 F50-F59 Behavioural syndromes associated with physiological disturbances and physical factors

These are a diverse group of disorders where mental symptoms and physiological disorders co-exist[237]. This thesis will consider F50: Eating Disorders, as these may be associated with poor body image seen in cancer survivors[246,247], but not other disorders within this category such as sexual

dysfunction, as these are both relatively rare, and also complex, and thus were felt to be out with the remit of this work.

1.9.2.7 F60-F69 Disorders of adult personality and behaviour

These are a group of disorders characterised by clinically significant abnormal or maladaptive patterns of behaviour[237]. These conditions are common, and can be challenging to treat[248]. They have been included in this work, with the exceptions of F64: Gender Identity Disorders and F66: Psychological and behavioural disorders associated with sexual development and orientation, which have been excluded due to marked concerns from the psychiatric community that these should not be conceptualised as mental disorders[249,250].

1.9.2.8 F70-F79 Mental retardation

These are disorders of cognitive function[237]. Like organic disorders, they have been excluded from this work as they have already been relatively well studied[239–241].

1.9.2.9 F80-F89 Disorders of psychological development

These are disorders which are associated with delayed maturation of the nervous system, and include dyspraxia and dyslexia[237]. Because these conditions often diminish with age, they have been excluded from this thesis.

1.9.2.10 F90-F98 Behavioural and emotional disorders with onset usually occurring in childhood and adolescence

This is a diverse group of conditions which have onset in early life, but which may or may not persist into adulthood[237]. This thesis will include F90: Hyperkinetic disorders, F91: Conduct disorders (including oppositional defiant disorder; ODD), F92 Mixed disorders of conduct and emotions and F93: Emotional disorders with onset specific to childhood. The other listed disorders are a heterogeneous group which are generally not seen in adults, and have thus been excluded from this work.

1.9.2.11 F99-F99 Unspecified mental disorder

Any other mental disorder which does not otherwise fit within the ICD-10 classification[237].

1.10 Evidence Gaps

There is evidence from CYP with other conditions that physical and mental ill health are linked. Issues such as stress, changes in appearances and bullying are all likely to be encountered by CYP with cancer, and it therefore follows that they will also be at considerable risk of mental health problems. Despite this, there are many gaps in the current evidence base surrounding psychiatric late effects of CYP's cancer.

Although a number of studies have reported increased psychiatric and psychological morbidity in survivors of CYP's cancers[155,157,160–162,172], none include diagnoses from primary care, although there are studies looking at prescribing patterns[156,165], which do include primary care data.

Data from primary care on diagnoses, referrals and treatments would provide a much more robust estimate of the prevalence of psychiatric morbidity within survivors of CYP's cancers, and potentially allowing identification of particular conditions which are more prevalent in this group. Using data linkage techniques, it may then be possible to identify particular patients groups who are at increased risk of mental health problems, based on age at diagnosis, cancer type and treatment modality.

The majority of studies looking at mental health of CYP's cancer survivors rely on self-reported data[155,157,160–162,172]. The evidence base would be greatly enhanced by the inclusion of clinician-diagnosed mental illness, particularly given the known difficulties with self-reporting of psychiatric symptoms[158,159].

1.11 Aims & Objectives

This chapter has described the rationale for this project, and in particular the evidence gaps described in section 1.10 have guided the selection of aims and objectives. Section 1.9.2 gives details on how mental health disorders are classified, and explains which ones have been included in this work and why.

This work aimed to investigate the prevalence and spectrum of mental health disorders in long-term survivors of children and young people's cancers. The YSRCCYP was used to identify cancer survivors, whilst using datasets from NHS Digital and primary care to determine contacts with secondary and primary healthcare services respectively, relating to psychiatric disorder.

The objectives of this project were:

1. To describe what is currently known about the mental health of CYP's cancer survivors.

2. To use data linked from secondary care to determine the prevalence of mental health disorders requiring secondary care input in CYP's cancer survivors and compare this to the background population.

3. To see whether any change in prevalence of mental health difficulty in CYP's cancer survivors over time mirrors that seen in the background population.

4. To attempt to identify groups who have particularly high prevalence of mental health disorder requiring secondary care input

5. To use data linked from primary care to determine the prevalence of any diagnosed mental health disorder in childhood cancer survivors and compare this to the background population.

6. To attempt to identify groups who have particularly high prevalence of specific mental health disorders, based on primary care records.

7. To explore whether sub-fertility and fertility preservation impacted on prevalence of mental health difficulties.

Chapter 2 Systematic Review of the Literature

2.1 Introduction

The introduction to this area and rationale for study is explained in detail in Chapter 1: Introduction. Section 1.1.2: Epidemiology gives an overview of the epidemiology of cancer in children and young people, whilst Section 1.5: Late Effects of Childhood and Young Adult Cancer and Section 1.6: Physical Late Effects describe some of the long-term consequences of a cancer diagnosis and its treatment in this age group. Section 1.7: Late Effects on Mental Health gives some introduction to the topic of psychological and psychiatric late effects. In order to fully evaluate the existing literature and explore potential gaps which could be the target of this thesis, a systematic review was carried out.

2.2 Methods

In April 2017, a standard systematic review was performed of the PubMed, Embase/OVID, CINAHL and Web of Science databases using the following strategy:

(child OR children OR childhood OR teen* OR adolescent* OR "young adult")

AND (cancer OR leukaemia OR tumour OR tumor)

AND survivor

AND "mental health" or "mental illness" or "psychiatric" or "psychological" or "emotional" or "behavioural" or “behavioral”

AND "late effects" or "long term"

Each abstract was screened by 2 separate individuals to decide whether it met the criteria for inclusion. Where the 2 initial reviewers disagreed on whether or not to include the paper, a third individual reviewed the abstract separately. As well as the author of this thesis, 2 medical students, Emily Hughes and Kristian Dye, were involved in the screening, and were given authorship of the published work as described in the declarations at the beginning of the thesis. Most ineligible papers were able to be excluded at the abstract screening

stage, however there were some papers where the abstract included insufficient detail to determine exclusion and these therefore proceeded to full text review before exclusion.

The reference lists of each included study were also reviewed to identify additional papers which may not have been picked up in the original search but which may have been relevant.

2.2.1 Inclusion criteria

Papers looking at the prevalence of mental health problems in long term survivors of CYP's cancer were included. Papers focussing on patients who had undergone haematopoietic stem cell transplant (HSCT) for non-malignant conditions were also included, on the basis that these individuals would have been exposed to intensive chemotherapeutic agents in their conditioning regimes, and would therefore be at risk of similar LEs to cancer survivors.

2.2.2 Exclusion criteria

Papers focussing only on cognitive function were excluded, as this issue has already been relatively well described in the literature, and was therefore not a key focus of this work. Papers which included patients less than 5 years from diagnosis were excluded, as these individuals would not be classed as "long term" survivors. Papers which included adult patients and did not report separately on outcomes for CYPs were also excluded. Conference abstracts which did not provide sufficient information to ensure inclusion criteria were met were also excluded, as were papers where the full text was not available in English language.

2.3 Results

The initial search returned 1530 papers: 320 papers underwent full text review, and 64 were included in the final review. Three additional papers were identified from screening reference lists of included studies. Figure 2.1 describes the screening and identification of studies, based on the PRISMA method[251].

Figure 2.1 PRISMA diagram showing study selection process.

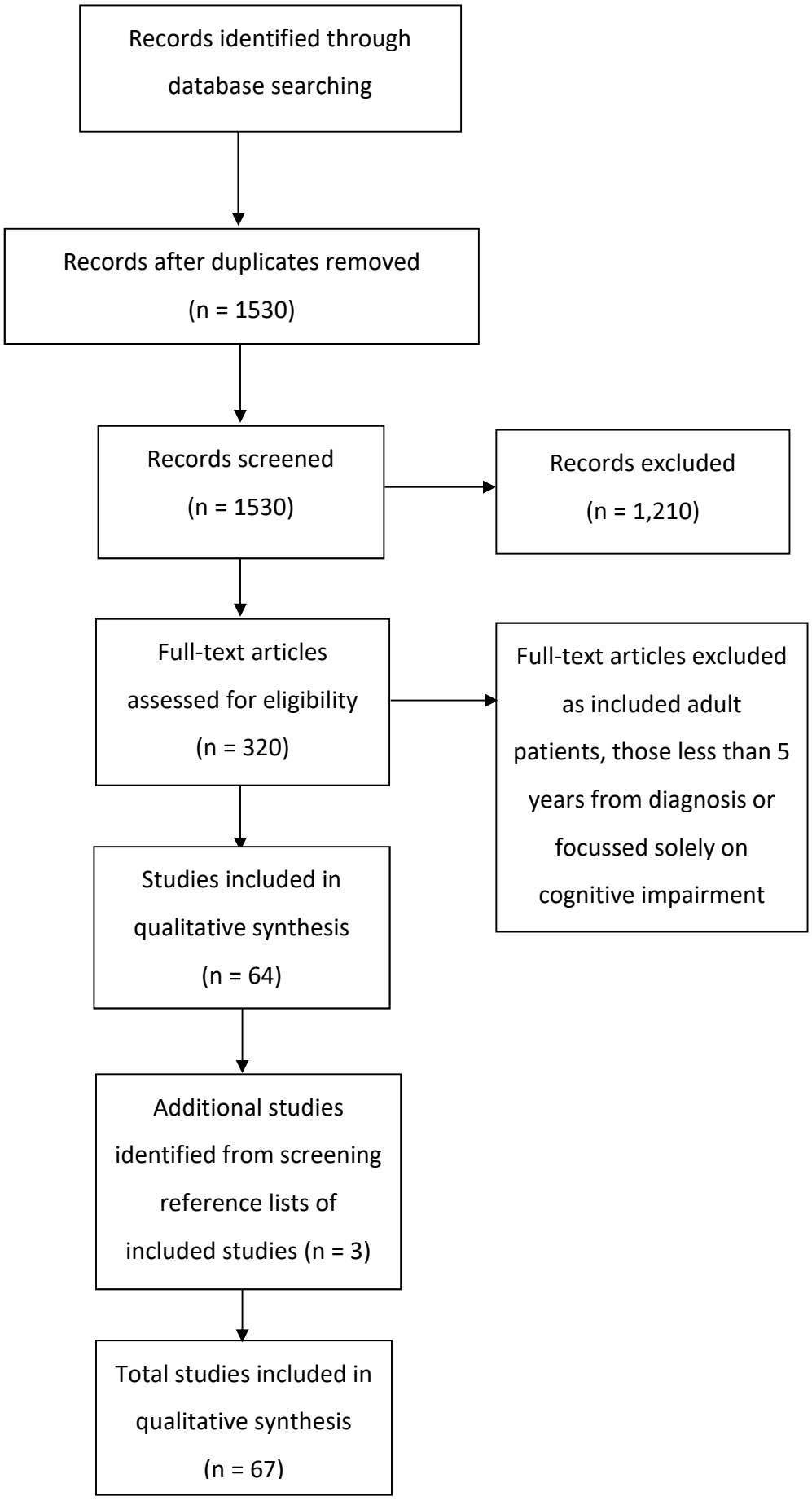


Table 2.1 describes the 67 included studies and gives details of their findings. The country of the study and year of publication, study and control groups, outcomes and results, as well as strengths and limitations, are described.

The qualitative synthesis suggested increased mental health problems in survivors of CYP's cancers, with some papers finding that as many as half of survivors report a psychiatric diagnosis at some point since treatment and around a third report a current psychiatric diagnosis[252]. Difficulties were still noted in patients who had completed treatment more than 30 years previously[253].

Table 2.1 Summary of included studies in the final synthesis.

Abbreviations: 15D, 15 Dimensional Health Related Quality of Life Instrument. ASPP, Assessment of Social Perspective-Taking Performance. ASR, Adult Self Report. AYA, adolescent and young adult. BFS, Behaviour and Feeling Survey. BPI, Behaviour Problems Inventory. BSI, Brief Symptom Inventory.BSI-18, Brief Symptom Inventory (18 question form). CBCL, Child Behaviour Checklist. CDI, Children's Depression Inventory. CES-D, Centre for Epidemiological Studies – Depression Scale. CISS, Coping Inventory for Stressful Situations. DIA-X, Diagnostic Expert System for Mental Disorders, DSM-IV, Diagnostic and Statistical Manual of Mental Disorders Fourth Addition. FRI, Family Relationship Index. GvHD, Graft versus Host Disease. GSI, Global Severity Index. HADS, Hospital Anxiety and Depression Scale. IES, Impact of Event Scale. IES-R, Impact of Event Scale – Revised version. IES-R-J, Impact of Event Scale – Revised version – Japanese language version. IWS, International Worry Scale. MINI, Mini-International Neuropsychiatric Interview. MOS-SSS, Medical Outcomes Study – Social Support Survey. PDS, Post-Traumatic Diagnostic Scale. PTSD, Post-Traumatic Stress Disorder. RAND-36, 36 item form developed by the Research And Development Corporation. RB, retinoblastoma. SCL-90-R, Symptom Checklist (90 item form) – Revised version. SF-36, Short Form Survey (36 item form). SI-PTSD, Structured Interview for Post-Traumatic Stress Disorder. YSR, Youth Self Report.

Citation	Country and Year of Study	Study group	Outcome	Key Result	Strengths & Limitations	Notes
Ahomäki *et al*[254]	Finland, 2015	13860 childhood and YA cancer survivors and 43392 sibling controls	Prevalence of psychiatric disorder	Mood disorders more common in childhood (HR 1.3; CI 1.1–1.7) and YA (1.3; CI 1.1–1.5) cancer survivors than in	+ Very large sample size	

				siblings. Neurotic/anxiety disorders, were slightly more common in childhood (HR 1.3; 1.0–1.7), and YA survivors (HR 1.2; 1.0–1.5) compared with siblings. Psychotic disorders slightly more common in childhood survivors (HR 1.4; 1.0–1.9) compared with siblings.	+ Physician-diagnosed problems - Only includes problems requiring hospital treatment - Sibling control group	
Ander *et al*[255]	Sweden, 2016	28 10-year survivors of adolescent cancer	HADS scores	29% reported possible anxiety and none reported possible depression	- Scoring system validated only in inpatients - Very small sample size	

Ashford *et al*[256]	USA, 2014	50 childhood brain tumour survivors, 40 siblings of brain tumour survivors, and 40 solid tumour survivors not receiving CNS-directed therapy.	Conceptual adaptive domain score, social adaptive domain score, practical adaptive domain score and general adaptive composite score	Brain tumour survivors scored lower than siblings ($p < 0.01$) and solid tumour survivors ($p < 0.04$) across all domains. There was no significant difference between solid tumour survivors and siblings. Global score average 96 for brain tumour survivors vs 107 for siblings and 106 for solid tumour survivors	+Use of validated scoring system - Use of siblings as control group	Note lower IQ in brain tumour survivors (although mean IQ still fell within the "average" range)
Bagur *et al*[252]	France, 2015	130 adult survivors of childhood non-leukaemia malignancies	Self-reports of psychiatric diagnosis	56.2% report at least one psychiatric diagnosis since their cancer diagnosis, including 35.4% with an ongoing disorder.	- Reliance on self-report - Lack of control group	
Boman *et al*[257]	Sweden, 2013	528 CNS tumour survivors	Body image scores	48% of females had a negative score compared to 31% of males ($p<0.00001$)	+ Use of validated	

				Body image was poorer in survivors with greater residual impairment	scoring system +Controls for confounding variables	
Brinkman *et al* (a)[161]	USA, 2016	3,893 survivors of cancer diagnosed <21 years of age	BPI scores	Treatment with ≥ 30 Gy CRT compared with treatment with < 30 Gy associated with greater odds of global symptoms (OR 3.2; 95% CI 1.2 - 8.4) and internalizing symptoms (OR 1.7; CI 1.0 - 2.8) Treatment with ≥ 300 mg/m2 anthracyclines compared no anthracycline treatment was associated with increased risk of internalizing symptoms (OR 1.9; CI 1.2 - 3.0)	+ Use of validated scoring system + Inclusion of patients in the “young adult” category - Lack of non-cancer-patient control group	

Brinkman *et al* (b)[155]	USA, 2013	4569 childhood cancer survivors	BSI-18 scores	Survivors with a mild-to-moderate medical condition at baseline were more likely to have persistent symptoms of depression (OR=1.6; CI=1.2–2.2), anxiety (OR=1.6; CI=1.1–2.5) and somatisation (OR=1.8; CI=1.2–2.9). Survivors who perceived their physical health to be worsening over time were more likely to have persistent symptoms of depression (OR=2.9; CI=2.0–4.1), anxiety (OR=3.4; CI=2.3–5.4) and somatisation (OR=4.4; CI=2.8–6.8) and more likely to have increasing symptoms of depression (OR=3.3; CI=2.4–4.5), anxiety (OR=3.0; CI=2.2–	+ Use of validated scoring system + Very large sample size allowing subgroup analysis + Longitudinal design - Lack of control group	

				4.0) and somatisation (OR=5.3; CI=3.9–7.4). Survivors who reported higher levels of cancer-related pain also had higher rates of persisting symptoms of depression (OR=2.1; CI=1.4–3.2) and somatisation (OR=3.3; CI=2.0–5.4) and higher rates of increasing somatisation (OR=2.4; CI=1.6–3.6). Change from being married to being single was associated with increased likelihood of persistent depressive symptoms (OR=2.3, CI=1.1–4.6).		

				Change to unemployed was associated with persistent somatic symptoms (OR=1.8, CI=1.2–2.8) Female survivors were more likely to report increasing somatisation (OR=1.6, CI=1.3–2.0).		
Brinkman *et al* (c)[258]	USA, 2013	10378 adult survivors of childhood cancer and 3206 sibling controls	Prescriptions of psychotropic medication (NB included analgesia)	22% of survivors reported psychotropic medicine prescriptions at baseline, compared to 15% of controls (p<0.001). 31% of survivors reported new prescription of psychotropic medication during the study period, compared to 25% of controls (p<0.001).	+ Very large sample size - Use of sibling controls - Inclusion of analgesics in the "psychotropic" category	Survey completed at baseline (2000), 2003, 2007 and 2011. Marked attrition with only 5982 survivors completing 2011 survey.

				Survivors were significantly more likely than siblings to be prescribed hypnotics/anxiolytics/sedatives (OR 1.64, CI 1.17–2.28) but not antidepressants, stimulants or neuroleptics	- No information on indication for prescription	
Brinkman *et al* (d)[259]	USA, 2014	9128 childhood cancer survivors and 3082 sibling controls	Self-reported suicidal ideation	Survivors were more 1.8-2 times more likely to report suicidal ideation at baseline and at each follow-up. Survivors were 2.6 times more likely than siblings to report recurrent suicidal ideation. Even after adjusting for depression, survivors with poor physical health were more likely to report suicidal	+ Very large sample size - Reliance on self-reported suicidal ideation - Use of sibling control group	

			All-cause mortality	ideation than those in good health. 6.4% of survivors died during the study period. 1.6% of deaths were due to suicide and 30% of those who completed suicide had previously reported suicidal ideation. Risk of all-cause mortality was greater in survivors with a history of suicidal ideation compared to those without (HR = 1.29, CI = 1.03-1.61). Survivors with a history of suicidal ideation had greater risk of death by external cause (HR = 2.37, 95% CI = 1.36-4.12)		

Castellino *et al*[260]	USA, 2005	443 black, 503 Hispanic and 7,821 non-Hispanic white adult survivors of childhood cancer	Self-reported mental health problems	Black survivors reported fewer mental health problems than white survivors (male OR 0.5; CI 0.3-0.8; female OR 0.6; CI 0.4-0.9). All black survivors were less likely than white to report anxiety (male OR 0.4; CI 0.2-0.9; female OR, 0.5; CI 0.2-0.9) and adverse mental health in at least one domain (male OR 0.5; CI 0.3-0.8; female: OR 0.6; CI 0.4-0.9). Male black survivors were also less likely to report adverse global mental health (OR 0.4; CI 0.2-0.8) and depression (OR 0.5; CI, 0.3-0.9).	+ Large sample size + Diverse population - Relies on self-report - Lack of control group	Reported results are after adjustment for social-economic status

Chou & Hunter[261]	Taiwan, 2009	98 survivors of childhood brain tumour or ALL	Quality of life scores	ALL survivors scored higher in all domains, p<0.001. Mean ranks; body image 62.95 for ALL vs 36.05 for brain tumours, psychological functioning 62.04 for ALL vs 36.96 for brain tumours; intimate relationships 55.80 for ALL vs 43.20 for brain tumours; social functioning 62.43 for ALL vs 37.57 for brain tumours.	+ Validated scoring systems - Lack of non-cancer control group - Relatively small sample size	
Cox *et al*[262]	USA, 2016	1189 childhood cancer survivors	Self-reported unmet care needs	25% of survivors reported no unmet care needs. Mostly commonly reported unmet needs were psycho-emotional (54 %), cancer-related information (51 %), care/support and health care system concerns (35%),	+ Large sample size - Reliance on self-report - Lack of control group	

				reported coping needs (41%) and surveillance-related needs (33%).		
D'Agostino *et al*[263]	USA, 2016	16,079 childhood cancer survivors and 3085 siblings	BSI-18 scores	Compared with siblings, survivors were less likely to be asymptomatic (62% vs 74%, p<0.0001), more likely to have comorbid distress (11% vs 5%, p<0.0001). Survivors of leukaemia (OR 1.34; CI 1.12-1.61), CNS tumours (OR 1.30; CI 1.05-1.61) and sarcoma (OR 1.26; CI 1.01-1.57) had a greater risk of comorbid distress than survivors of other solid tumours.	+ Use of validated scoring system + Very large cohort + Inclusion of subgroup analysis - Use of sibling controls	
Daniel *et al*[264]	USA, 2016	154 survivors of non-CNS childhood cancer	Time to fall asleep and duration of sleep	No difference in time to sleep or duration of sleep between survivors and controls.	+ Use of validated	

		and 170 age and sex matched controls	BSI-18 scores	Survivors with longer duration of sleep and greater reported fatigue also reported higher rates of anxiety, depression and somatisation.	scoring system + Controls unaffected by childhood cancer - Reliance on self-reporting of sleep times	
De Laage *et al*[253]	France, 2016	348 long term survivors of childhood cancer compared to the French general population	MINI scores IWS scores IES scores	Survivors experienced a higher prevalence of anxiety and mood disorders compared to controls, even a long time after diagnosis. Prevalence ratios; major depressive disorder 2.08, dysthymia 2.52, panic disorder 1.48, generalised anxiety disorder 1.49, agoraphobia 2.29	+ Use of validated scoring systems + Reference to population controls	

Deyell *et al*[265]	Canada, 2012	2,389 survivors childhood and young adult (dx <25) cancer and 23,890 randomly selected age- and gender-matched controls	Prescriptions of antidepressant medication	Survivors more likely to have filled a prescription for antidepressant medication (OR 1.21; CI 1.09–1.35) than controls. Females, young adults and very long term (>20 years) survivors had highest use of antidepressants.	+ Large cohort + Randomly selected controls - No information on indication for prescription	
Erickson & Steiner[266]	USA, 1999	40 long term survivors of childhood cancer	SI-PTSD scores	10% met the criteria for PTSD	+ Validated scoring system - Small sample size - Lack of controls	
Fidler *et al*[267]	UK, 2015	10 488 survivors of childhood cancer (results compared with	SF-36 scores in role emotional	Females more likely to be limited in all three questions (Q1 OR 1.6 95% CI 1.4-1.8;	+ Large scale study	

		Oxford Healthy Life Survey)	SF-36 scores in social functioning	Q2 OR 1.5 95% CI 1.3-1.7; Q3 OR 1.8 95% CI 1.6-2.0). Survivors of NHL (Q1 OR 1.4 95% CI 1.1-1.9; Q2 OR 1.4 95% CI 1.1-1.7; Q3 OR 1.6 95% CI 1.2-2.1), CNS tumours (Q1 OR 1.6 95% CI 1.4-2.0; Q2 OR 1.5 95% CI 1.2-1.7; Q3 OR 1.5 95% CI 1.2-1.8), and bone sarcoma (Q1 OR 1.7 95% CI 1.2-2.4; Q2 OR 1.4 95% CI 1.1-1.9; Q3 OR 1.5 95% CI 1.1-2.1) more likely to be limited for all questions compared to survivors of leukaemia.. Females more likely to report dysfunction in both domains (Q1 OR 1.5 95% CI 1.3–1.7; Q2 OR 1.5 95% CI 1.4–1.7).	+ Large non-cancer control group + Use of validated scoring systems + Includes analysis of most at-risk groups	

			SF-36 scores in mental health	Survivors of CNS tumours (Q1 OR 1.6 95% CI 1.4–1.9; Q2 OR 2.5 95% CI 2.1–2.9) and bone sarcomas (Q1 OR 2.0 95% CI 1.5–2.7; Q2 OR 3.0 95% CI 2.3–4.0) more likely to report dysfunction in both domains compared to leukaemia survivors. Survivors of soft tissue sarcomas more likely to report dysfunction when asked “Has your health limited your social activities?” compared to leukaemia survivors (OR 1.6 95% CI 1.2-2.0) Survivors who were female (ORs 1.2-1.7) or who had never worked or were unemployed (ORs 1.3-2.6)		

				were significantly more likely to report dysfunction in all 5 questions.		
Ford *et al*[268]	USA, 2015	470 retinoblastoma survivors and 2820 siblings of childhood cancer survivors	BSI-18 scores	Survivors significantly less likely to report global symptoms (standardised T score 43.7 vs 46.7, p<0.01), depression (standardised T score 46.1 vs 47.1, p=0.02), somatic distress (standardised T score 45.2 vs 48.2, p<0.01) and anxiety (standardised T score 44.6 vs 46.8, p<0.01) compared with siblings.	+ Large sample size + Use of validated scoring system - Use of sibling control group - Lack of differential results for those with bilateral RB	

Gianinazzi *et al*[160]	Switzerland, 2014	1602 survivors of childhood cancer and 703 siblings	Utilization of mental health services BSI-18 scores	No significant difference between survivors and siblings. However, of those with BSI-18 scores indicating distress, 34% of survivors accessed mental health services, compared to 20% of siblings ($p<0.001$) No significant difference between survivors and siblings.	+ Large sample size + Validated scoring system - Sibling control group	
Gunn *et al* (a)[269]	Finland, 2015	740 childhood brain tumour survivors and 3615 healthy siblings	Prevalence of psychiatric morbidity	Increased in survivors compared with siblings (HR 1.8; CI 1.4–2.5). Significantly increased risk for schizophrenia/delusional disorders (HR 2.2; CI 1.1–4.1), mood disorders (HR 2.3; CI 1.5–3.6), and	+ Physician-diagnosed problems - Sibling control group - Lack of inclusion of problems	

				neurotic/somatoform disorders (HR 1.9; CI 1.1–3.2).	treated in primary care	
Gunn *et al*(b)[270]	Finland, 2015	315 AYA brain tumour survivors and 3615 healthy siblings	Prevalence of psychiatric morbidity	No statistically significant increase in survivors compared with siblings	+ Physician-diagnosed problems + Specifically looks at AYAs - Sibling control group - Lack of inclusion of problems treated in primary care	
Gunn *et al* (c)[271]	Finland, 2016	21 childhood brain tumour survivors compared to general population controls	BDI scores	Only 4.8% of respondents scored highly enough to indicate any level of depression.	+ Use of validated scoring systems	

			15D scores	Survivors had worse scores in mobility (mean score 0.92 vs 1.0), vision (mean score 0.93 vs 0.98), hearing (mean score 0.91 vs 0.99), eating (mean score 0.96 vs 1.0), speech (mean score 0.84 vs 0.99), usual activities (mean score 0.82 vs 0.97), mental function (mean score 0.82 vs 0.93), and sexual activity (mean score 0.90 vs 0.96).	+ Population controls - Very small sample size	
Harila *et al*[272]	Finland, 2010	63 childhood cancer survivors compared to	RAND-36 scores	Survivors scored significantly better than general population on the subscales of role limitations due to emotional problems (mean score 91 vs 78, p = 0.030) and mental	+ Validated scoring system + Population controls - Small sample size	

				health (mean score 80 vs 74, p = 0.030)		
Hill *et al*	USA, 1998	110 survivors of childhood ALL (mean age 20.8 years) randomised to receive either 2400 centigray of cranial radiation with intrathecal methotrexate or intermediate dose systemic methotrexate with intrathecal methotrexate	Body image Psychological distress	Significantly poorer (MANCOVA 10.1 vs 7.9 p = 0.001) in patients treated with cranial radiation compared to those who did not receive cranial irradiation. Significantly greater (MANCOVA 8.6 vs 6.7 p = 0.049) in patients treated with cranial radiation compared to those who did not receive cranial irradiation.	+ Use of validated questionnaire - ALL patients no longer receive cranial irradiation, therefore less applicable to patients treated more recently. - Lack of non-cancer-patient controls	

Hoffmeister *et al*[273]	USA, 2016	1084 childhood HSCT survivors	Self-reported diagnosis of depression	18% of patients reported a diagnosis of depression (2% of these committed suicide during follow-up) Depression was more common in those who had HSCT transplant at 6-12 years (HR 2.29, CI 1.5–3.5, p = 0.0002) or 12-18 years (HR 3.63 CI 2.3–5.7, p<0.0001)	+ Large sample size - Reliance on self-report rather than clinical diagnosis	Multiple other risk factors including surgery post-transplant, obesity, non-sibling donor.
Honda *et al*[274]	Japan, 2011	32 childhood solid tumour survivors	CBCL scores YSR scores	Female survivors had significantly lower scores for externalizing (delinquent behaviour, aggressive behaviour) than population averages (mean score 11.37 ± 9.43 vs 14.35 ± 13.48, *p* = 0.003)	+ Use of validated questionnaires - Very small sample size	

			IES-R scores	12.5% had scores ranging from borderline to clinical in internalizing, externalising and/or total problems. Only one child had evidence of post-traumatic stress and the mean score was very low at 4.0 (median 0.5, standard deviation 9.08).		
Hörnquist *et al*[247]	Sweden, 2015	528 survivors of CNS tumours and 995 randomly selected controls	Proportion with negative self-esteem surrounding body image Proportion with negative self-esteem surrounding peers	More likely in survivors (30.1%) than controls (17%) More likely in survivors (30.1%) than controls (17%)	+ Use of random controls + Use of validated questionnaire	

			Proportion with negative self-esteem surrounding work	More likely in survivors (22.2%) than controls (7.4%)		
Hudson *et al*[275]	USA, 2015	6875 childhood cancer survivors and 2351 siblings	Reported adverse mental health (as per BSI-18)	More likely in survivors than siblings, (PR 1.66; 95% CI 1.52 to 1.80)	+ Use of well validated scoring system - Use of survivors as control group	Did not increase with age. Any history of brain surgery associated with adverse mental health, as well as other severe chronic impairment
Kamibeppu *et al*[276]	Japan, 2015	185 childhood cancer survivors	IES-R-J scores	20.7% of survivors scored above the cut off for PTSD.	+ Use of validated	

				Female survivors, those who were older at the time of diagnosis and those suffering from late effects were at higher risk of PTSD. Better family functioning was associated with decreased risk of PTSD (β = −.27, p=0.001) as was increased satisfaction with social support (β = −.1, *p*=0.026).	scoring system - Lack of control group	
Krull *et al*[277]	USA, 2009	1656 survivors of childhood cancer	Adult obesity Adult physical inactivity	More prevalent in those who were socially withdrawn (OR 1.5, 95% CI 1.1-2.1) or used stimulant drugs (OR 1.9, 95% CI 1.1-3.2) during adolescence More prevalent in those socially withdrawn in	+ Large study size +Adjusted for cancer diagnosis, cancer therapy, sex, age, and	Estimates were adjusted for cancer diagnosis, cancer therapy, sex, age, and history of

			Adult smoking Adult sunscreen use	adolescence (OR 1.7, 95% CI 1.1-2.5) More prevalent in those with adolescent antisocial behaviour (OR 2.6, 95% CI 1.6-4.2) Less prevalent in those using stimulant medication during adolescence (OR 0.4, 95% CI 0.2-0.8).	history of special education - Self-reported health behaviours - Lack of details on which groups are at risk of psychiatric problems during adolescence	special educational needs
Lehmann *et al*(a)[246]	USA, 2016	87 adult survivors of non-CNS malignancy diagnosed between the ages of 5 and 18y	Body image scale, body dissociation scale, sexual satisfaction and	No significant difference between survivors and controls in any domain,	+ Use of validated scoring systems with good reliability	

		compared with 400 healthy controls.	status satisfaction scores		- Removal of questions referring to previous cancer treatment	
Lehmann *et al* (b)[278]	Sweden, 2014	28 10-year survivors of childhood cancer	Self-reported psychological problems Self-reported negative feelings about appearance	32% reported psychological problems, including feeling inferior or negative about themselves, useless and depressed. 46% described physical sequalae which interfered with and caused negative feelings about their looks.	- Very small sample - Relies on self-report	
Lesko *et al*[279]	USA, 1992	51 acute leukaemia survivors treated with chemotherapy alone and 22 treated with	BSI scores	Rates of distress were higher in both groups that the general population but this did not meet a psychiatric threshold.	+ Validated scoring system	

		chemotherapy and BMT		There was no difference between groups.	- Very small sample size - Lack of non-cancer-patient control group	
Liu *et al*[280]	USA, 2016	162 survivors of childhood ALL	Connors Self Report Scale Scores Parent-reported Diagnostic Interview for Children and	Significantly more survivors self-reported inattention (27.7%), hyperactivity/impulsivity (25.8%) and oppositional behaviour (20%) than the expected rate of 10% (all $p<0.0001$) Significantly higher frequencies of GAD (3.2% vs. 1.1%), OCD (10.3% vs. 1-3%), Simple/Social Phobias (22.3% vs. 15.8%) and ODD (15.9%	- Use of parent and patient report measures rather than diagnoses	

			Adolescents Scores	vs. 8.3%) than the general population (all p<0.05)		
Löf *et al*[281]	Sweden, 2009	51 stem cell transplant survivors and 152 healthy controls	HADS scores	35% of survivors reported problems with anxiety and depression, compared to 10% of controls. 14% had problems with both anxiety and depression, 16% with anxiety only and 6% with depression only.	- Scoring system only validated in inpatients.	
Lown *et al*[282]	USA, 2008	10 398 childhood cancer survivors, 3034 siblings and 4774 respondents from the National Alcohol Survey	Likelihood of risky drinking Likelihood of heavy drinking Risk factors for heavy drinking	Less likely (OR = 0.9; CI 0.8–1.0) in survivors Less likely (OR = 0.8; CI 0.7–0.9) in survivors Among survivors, symptoms of depression, anxiety or somatization, fair/poor health,	+ Large cohort + Inclusion of non-cancer-patient controls - Reliance on self-reported	Among survivors, symptoms of depression, anxiety or somatization, fair/poor health, activity

				activity limitations and anxiety about cancer were associated with heavy drinking. Cognitively compromising treatment, brain tumours and older age at diagnosis were protective	alcohol consumption	limitations and anxiety about cancer were associated with heavy drinking. Cognitively compromising treatment, brain tumours and older age at diagnosis were protective
Lund *et al* (a)[162]	Denmark, 2013	7085 childhood cancer survivors and 13105 matched sibling controls	Hospital contacts for mental health problems	Excess risk for inpatient contact for mental disorders was 0·92 contacts per 1000 person-years for male survivors of childhood cancer	+ Use of in- and out-patient contacts	Data on inpatient-only contacts from 1975–1994, data on all

				(CI 0·30–1·54) and 0·84 for females (0·24–1·46). Excess risk for in- and out-patient contacts was 2·25 contacts per 1000 person-years for males (CI 1·45–3·04) and 1·26 for females (0·26–2·26).	- Use of sibling controls - Lack of data from primary care setting	contacts from 1995-2009
Lund *et al*(b)[156]	Denmark, 2015	5452 survivors of childhood cancer and 144570 age- and sex-matched controls	Antidepressant use	Survivors were at increased risk of being prescribed antidepressants (HR 1.4; CI 1.3–1.5). Risk was higher for stem cell transplant recipients (HR 1.9; CI 1.2–3.1) and those with solid tumours in the extremities (HR, 1.8; CI 1.4–2.3)	+ Very large sample size + Matched control group - Lack of information on reason for prescription	
Mackie *et al*[283]	UK, 2000	102 survivors of childhood ALL/Wilms	Rates of diagnosed	No significant difference between groups	+ Use of validated	

		tumour and 102 healthy controls	psychiatric disorder Work and educational performance scores Adult personality functioning assessment scores	No significant difference between groups Higher scores (poorer functioning) for cancer survivors in domains of love/sex relationships (mean difference 0·87, CI 0·53-1·22), friendship (0·37, CI 0·07–0·67), non-specific social contacts (0·40, CI 0·20–0·60), and day-to-day coping (0·35, CI 0·14–0·57)	scores for work, education and personality function scores - Only included white survivors, therefore not generalizable to other groups - Diagnosed psychiatric disorder based on interviews rather than	

					physician diagnosis	
Maurice-Stam *et al*[284]	The Netherlands, 2013	353 childhood cancer survivors aged 18-30 who were more than 7 years from completion of treatment	RAND-36 scores	Survivors of brain tumors had a lower score on psychosexual development (β = –0.89, p < 0.05) than survivors of leukemia/lymphoma. Having been treated with radiotherapy was negatively related to Social development (β = –3.12, p <0.01) and to psychosexual development (β = –1.14 p < 0.05). Combination chemo- and radiotherapy was negatively associated with psychosexual development (β = -1.21, p < 0.001). Longer treatment	+ Use of validated scoring system - Lack of control group	

				duration was negatively related to social development (β = -.05, p < 0.01)		
Michel *et al*[285]	Switzerland, 2010	987 adult (>20) survivors of childhood cancer	BSI scores	24.6% (CI 21.9-27.3%) of survivors scored highly on 2 or more domains or on the global severity index. Women (OR=1.88), only children (OR=2.09) and immigrants (OR=1.96) were more likely to report high distress than men, those with siblings, and those born in Switzerland.	+ Use of validated scoring system + Large sample size - Lack of control group	
Milam *et al*[172]	USA, 2015	193 long term survivors of childhood cancer	Self-reported substance use in past 30 days	Prevalence was 11% for tobacco, 25% for alcohol and 14% marijuana. 16% of the cohort used at least 2 substances.	- Reliance on self-reporting - Lack of control group	Alcohol use referred specifically to binge drinking

Oancea *et al*[286]	USA, 2014	1863 long term (> 10 years) childhood cancer survivors	BSI-18 scores	15.1%. of survivors reported an elevated level of global emotional distress; 11.7% reported elevated levels of anxiety, 15.0% reported elevated levels of depression and 17.8% reported elevated levels of somatization. Survivors who completed education prior to college had more distress than those who completed college or post-graduate education (OR 1.65; CI, 1.10–2.48). Survivors unable to work due to illness/disability had more distress than survivors who were either working or not working by choice e.g. students, retired (OR 1.83; CI	+ Use of validated scoring system - Lack of control group	

				1.01–3.34). Survivors without medical insurance had more distress than those with private medical insurance (OR 1.60; CI 1.11–2.32).		
Ozono *et al*[287]	Japan, 2010	88 survivors of childhood cancers, 87 mothers and 72 fathers of survivors	CDI scores	Mean scores of 9.8 (SD 6.0), 12.4 (SD 5.8) and 15.1 (SD 7.7) were found from children from “supportive”, “intermediate” and “conflictive” families, respectively (p=0.02).	+ Use of validated scoring system - Small sample size - Lack of control group	Family functioning calculated based on FRI scores. NB not discrete family clusters.
Poretti *et al*[288]	Switzerland, 2004	21 survivors of craniopharyngioma	Reported emotional functioning YSR scores	14% reported mood swings 42% had clinically elevated scores on the total behaviour	- Very small sample size - Tool used in patients up to 22 but only	YSR scores only obtained for 12 patients

				problems scale, 50% on the internalizing behaviour problems scale, and 17% on the externalizing behaviour problems scale.	validated in <18s - Lack of control group	
Prasad *et al*[240]	USA, 2015	2589 survivors of adolescent and young adult cancer, 3603 survivors of childhood cancer and 390 siblings	BSI-18 scores	Survivors diagnosed as adolescents reported greater anxiety (OR 2.00; CI 1.17-3.43), somatization (OR 2.36; CI 1.55-3.60) and depression (OR 1.55; CI 1.04-2.30), than siblings.	+ Very large sample size + Use of validated scoring system - Use of sibling control group	
Rebholz *et al*[289]	Switzerland, 2012	1,049 childhood (dx < 16 years) cancer survivors now aged 20-40	Frequency of alcohol consumption	Higher (OR = 1.7; CI 1.3–2.1) in survivors compared to background population	+ Use of population-based controls	

			Likelihood of binge drinking	More likely (OR = 2.9; CI 2.3–3.8) in survivors	- Reliance on self-report	
Recklitis *et al*[290]	USA, 2006	226 adult survivors of childhood cancer	Self-reported suicidal ideation	Reported by 12.8% of survivors (more likely in survivors who were younger at diagnosis, those who had had cranial irradiation and those with symptoms of depression)	+ Use of validated questionnaires - Lack of control group	
Sanders *et al*[291]	USA, 2009	214 survivors of childhood HSCT plus an age and sex-matched group of controls	SCL-90-R scores	Survivors were more likely to be depressed (p=0.03) than controls	+ Use of validated scoring system - Controls related in some way to survivors - Raw scores on SCL-90-R	Controls were either friends or siblings of survivors

					not provided; p value only given	
Schapiro *et al*[292]	USA, 2015	482 childhood rhabdomyosarcoma survivors and 393 sibling controls	BSI-18 scores SF-36 scores	Survivors had higher rates of depression (13.3% vs. 8.1%, p=0.020) and anxiety (7.9% vs. 4.4%, p=0.038) than siblings. Survivors reported poorer emotional functioning (19.2% vs. 13.5%, p=0.030) and greater role limitation due to emotional problems (21.3% vs. 13%, p=0.002) than siblings.		
Schultz *et al*[293]	USA, 2007	2,979 survivors and 649 siblings of cancer survivors aged 12-17	BPI scores	Survivors were 1.5 times (CI 1.1 - 2.1) more likely than siblings to have symptoms of depression/anxiety and 1.7	+ Use of validated scoring system	

				times (1.3 - 2.2) more likely to have antisocial behaviours.	- Use of sibling controls	
Seitz *et al*[245]	Germany, 2010	820 young adult survivors of childhood cancer and 1027 healthy, age-matched controls	HADS scores DIA-X interview scores	22.4% of survivors had clinically relevant scores compared to 14.0% of controls (ORs 1.77; CI 1.39–2.26). Posttraumatic stress was more likely in male (OR 3.92, CI 1.80–8.51) and female (OR 3.83, CI 2.54–5.76) survivors than controls. 24.3% survivors fulfilled the diagnostic criteria for at least one DSM-IV diagnosis including PTSD, depression and/or anxiety, compared to only 15.3% of controls (OR 1.77; CI 1.28–2.45)	+ Large sample size + Controls unaffected by cancer - HADS validated for use in inpatients	DIA-X interviews only carried out involving consenting participants who had elevated HADS scores.

Stuber *et al*[294]	USA, 2010	6542 childhood cancer survivors and 368 sibling controls	PTSD symptoms	9% of survivors reported symptoms of PTSD compared with 2% of siblings (OR 4.14; CI 2.08–8.25). PTSD was more likely in survivors treated with more intensive treatment (OR 1.36; CI 1.06–1.74) and those who received cranial radiotherapy before the age of 4 (OR 2.05; CI 1.41–2.97).	+ Very large sample size - Sibling control group - Reliance on self-report rather than clinical diagnosis	
Sun *et al*[295]	USA, 2011	1065 long-term HCT survivors, plus a sibling control group	BSI-18 scores	22% of survivors and 8% of siblings reported adverse psychological outcomes. Risk of distress was increased in survivors with active GvHD, self-reported poor physical health and low household income.	+ Large sample size + Validated symptom score - Sibling control group	

Sundberg *et al*[296]	Sweden, 2009	246 young adult survivors of childhood cancer	Self-reported negative consequences of childhood cancer	9% reported concerns about disease recurrence or further malignancy. 4.5% reported low self-confidence. 3.5% reported distressing memories. 3% reported hospital anxiety. 3% reported low mood. 2% reported anxiety. 2.5% reported other mood disturbance. 15% reported difficulties as a result of altered body appearance e.g. scars, poor hair quality, prostheses	- Reliance on self-report rather than clinical diagnosis - Lack of any form of control group	

Teall *et al*[297]*vv*	Canada, 2013	28 survivors of childhood/adolescent lower limb bone tumours	CES-D scores, ASPP scores, MOS-SSS scores and BFS scores	Overall scores were not significantly different to reference sample groups, although the survivors scored more highly for positive social interactions (mean scores 84.88 vs 69.8, p=0.003), lower for depression (mean scores 7.39 vs 12.51, p=0.005) and more highly for intelligence (mean scores 3.41 vs 3.11, p=0.009)	+ Use of multiple validated scoring systems - Very small sample size	Reference groups were general youth population, college population, HIV +ve patients and cancer patients.
van der Geest *et al*[298]	The Netherlands, 2013	628 childhood cancer survivors and 440 healthy controls	HADS scores	No significant difference between survivors and controls overall, however survivors who had had cranial radiotherapy had a significantly higher HADS score than the control group (mean score 8.3±6.6 vs	- Scoring system validated only in inpatients - Mean score for controls not given	

				6.6±5.3, p=0.05) or other survivors (p=0.01)		
van Dijk *et al* (a)[299]	The Netherlands, 2009	148 retinoblastoma survivors (compared to a reference sample)	CBCL scores	Young (<12y) and adolescent male RB survivors reported to have higher rates of internalising problems compared with reference group (young mean difference 6.2, p = 0.037; adolescent mean difference 5.6, p = 0.030). Young (<12y) and adolescent male RB survivors reported to have higher rates of somatic problems compared with reference group (young mean difference 6.1, p=0.011; adolescent mean difference 3.6, p=0.047). Young female RB survivors reported to have	+ Use of validated scoring system - Lack of details on reference sample - Relatively small sample meaning sub-group analysis may be unreliable	

				more somatic problems compared with reference group (mean difference 7.7, p=0.013).		
			YSR (adolescent self-report) scores	Adolescent female RB survivors reported fewer externalising problems (mean difference 3.8, p=0.045), especially rule-breaking (mean difference 1.8, p=0.034) and aggressive behaviour (mean difference 2.5, p=0.022), than the reference sample; they also reported fewer thought problems (mean difference 2.4, p=0.004).		
			ASR (adult self-report) scores	Adult male RB survivors reported fewer thought problems (mean difference		

				1.3, p=0.047) than the reference group. Adult female RB survivors reported more somatic problems (mean difference 1.9, p=0.048) than the reference group, but fewer total problems (mean difference 3.3, p=0.025), particularly externalising problems (mean difference 2.8, p=0.024), aggressive behaviour (mean difference 1.3, p=0.038) and intrusive behaviour (mean difference 2.2, p=0.000)		
van Dijk *et al* (b)[300]	The Netherlands, 2009	117 retinoblastoma survivors compared to a reference sample	CISS scores	Survivors were less likely to employ the emotion-oriented coping strategy than the reference cohort (mean scores 27.57 vs 37-42 for adult	+ Use of validated scoring system	

			YSR/ASR total problem score	females, 25.06 vs 34-38 for adult males, 25.50 vs 48.38 for adolescent females and 28.40 vs 39.62 for adolescent males. All other strategies were used similarly. Adolescents who experienced reduced social support reported more total problems (β = -0.357). In adults, increased exposure to stressful life events (β = 0.24), more emotion-oriented coping (β = 0.534) and lower social support (β = -0.188) were associated with greater total problem scores. Adolescents with reduced social support (β = -0.447) and	- Lack of details on reference sample - Relatively small sample meaning sub-group analysis may be unreliable	

			YSR/ASR internalising behaviour score	decreased disease acceptance (β = -0.396) reported higher internalizing problems. Adults with lower scores on disease acceptance experienced more internalizing problems (β = -0.156). Increased exposure to stressful life events (β = 0.265), more emotion-oriented coping (β = 0.448) and lower social support (β = -0.309) were also associated with higher internalising behaviour scores.		
Vuotto *et al*[157]	USA, 2017	5021 survivors of childhood cancer	BSI-18 scores	Depression was more prevalent in survivors with endocrine conditions (RR1.3, 95% CI 1.1-1.6) and pulmonary conditions (RR 1.4,	+ Use of validated scoring systems	

			PDS scores	95% CI 1.1-1.7). Anxiety was more prevalent in survivors with cardiac conditions (RR=1.5, 95% CI 1.2-1.8) and pulmonary conditions (RR 1.6, 95% CI 1.3-.2.0). Post-traumatic stress symptoms were more likely in patients with cardiac (RR 1.3, 95% CI 1.2-1.5), endocrine (RR 1.3, 95% CI 1.2-1.5) and pulmonary conditions (RR 1.4, 95% CI 1.2-1.6).	+ Large sample size allowing subgroup analysis - Lack of control group	
Wenninger *et al*[301]	Germany, 2007	164 childhood cancer survivors	BSI-18 scores PDS scores	17% of the study sample were identified as clinically distressed, compared to 10% of the general population. 14% of cohort had scores indicative of clinically	+ Use of validated scoring system - No control group, just	

				significant PTSD (26% of solid tumor survivors vs 11% of leukemia, Hodgkin lymphoma and non-Hodgkin lymphoma survivors, $p = 0.027$).	use of population norms for comparison	
Zebrack *et al* (a)[302]	USA/Canada, 2007	2,778 survivors of childhood or adolescent solid tumours and 2,925 sibling controls	BSI-18 scores	Both survivors and siblings reported lower scores than population norms.	+ Use of validated scoring system + Large sample size - Use of sibling control group - Lack of detail on population norms, other than that these were	20% of sample had undergone amputation as part of treatment

					higher than participant scores	
Zebrack *et al* (b)[303]	USA, 2004	1101 brain tumour survivors and 2817 sibling controls	BSI-18 scores	11% of survivors had scores indicating clinically significant distress, compared to 5% of siblings.	+ Very large sample size + Use of validated scoring system - Use of sibling control group	
Zebrack *et al* (c)[304]	USA, 2002	4914 survivors of childhood haematological malignancy and 2446 sibling controls	BSI scores	5.4% of survivors reported symptomatic depression, compared with 3.4% of siblings. 12.7% of survivors reported somatic distress, compared with 8% of siblings.	+ Very large sample size - Use of sibling control group	

Zeltzer *et al*[305]	USA & Canada, 2015	7147 survivors of CYP (<21yrs) cancer and 388 siblings	BSI-18 scores	Survivors reported higher scores of global distress than siblings (mean scores 49.17 vs 46.64), but both groups scored lower than population averages.	+ Very large sample size + Use of validated scoring system - Use of sibling control group	
Zevon *et al*[306]	USA, 1990	46 survivors of childhood ALL with a control group of lymphoma survivors	Wellbeing scores Stress reaction scores	Those who received cranial irradiation had lower scores than those who received only intrathecal methotrexate ($F=4.49$, $p<0.05$). Significantly higher in female (but not male) ALL survivors than controls	+Use of validated questionnaire - Lack of non-cancer-patient controls - Raw scores not reported	

Zuzak *et al*[307]	Switzerland, 2008	28 survivors of low-grade cerebellar astrocytoma	Self-reported behavioural problems	33% reported behavioural problems	+ Use of validated questionnaire - Very small sample size	

2.3.1 Mental Health of CYP's cancer Survivors

A wide variety of problems were reported. These included difficulties with interpersonal relationships[283], increased somatic distress/somatisation[155,295,299,302–304], poor self-esteem[247], depression and other mood disorders[245,254,293,302,303,255,265,278,280,281,288,291,292], anxiety and other neurotic disorders[255,292,293,295,303,304], antisocial behaviour[277,293], PTSD[244,266,276,292,301], schizophrenia and other psychotic disorders[255,269], poor body image[281], difficulties fulfilling expected roles due to emotional disturbance[269], behavioural problems[307], mood swings[288], ODD[277], drug and alcohol misuse[172,289], suicidal ideation[259,290] and unmet emotional and coping needs[262].

One large study of hospital contacts found survivors of CYP's cancers were more likely to have both in- and out-patient assessment and treatment for mental health problems[162]. However, another study found that CYP's cancer survivors were more likely to access healthcare for mental health problems than siblings with the same problems[160]. It is therefore difficult to know whether increased hospital contact truly represents an increase in prevalence, or merely an increased likelihood of seeking help.

Two large studies investigated prescriptions amongst CYP's cancer survivors. One found increased prescribing of antidepressants[156] and another increased prescribing of psychotropic medication in general[258] amongst CYP's cancer survivors compared to the general population. Interestingly, the study reporting increased general psychotropic medication use did not note an increase in prescribing of antidepressant drugs[258]. Unfortunately, a reliance on self-reported data in one study and a lack of information on indications for prescriptions in the other mean that it is difficult to infer whether these increases in prescriptions truly represent increased prevalence of mental ill health. Furthermore, the study looking at overall psychotropic prescribing included analgesics in their defined "psychotropic" medications. Given the prevalence of chronic pain in cancer survivors, this makes the results challenging to interpret[168].

2.3.1.1 Risk Factors for Poor Mental Health in Survivors

Literature was available not only on the mental health problems and difficulties faced by some CYP's cancer survivors, but also on factors which appeared to be associated with increased risk of mental ill health.

2.3.1.1.1 Treatment

A number of studies reported on the effects of different treatment modalities, including chemotherapy, radiotherapy and surgery, on mental health outcomes. Cranial irradiation[161,298,306,308], particularly at an early age[244], treatment with high doses (≥ 300 mg/m^2) of anthracyclines[295] and more intense treatment generally[244] were all associated with greater likelihood of mental ill health, including increased PTSD risk. These differences were noted in older studies, which were carried out when cranial irradiation was a routine part of ALL treatment, but also in more modern studies. However, only 2 of these 5 studies also looked at a non-cancer control groups. Additionally, patients who had undergone brain surgery also reported more adverse mental health outcomes[275].

Results of a small and somewhat dated study suggest that leukaemia survivors treated with BMT had no greater risk of distress than those treated with chemotherapy alone[279]. However, timing of BMT was important, with another, much larger, study finding depression risk higher in survivors who underwent transplant in their teenage years than those transplanted as younger children[273].

2.3.1.1.2 Pathology

Multiple studies investigated results for survivors of different tumour types. Evidence from several robust, large-scale studies indicates that solid tumour survivors (including survivors of CNS tumours) appeared to have poorer mental health outcomes than survivors of haematological malignancy. Although some of these studies used scores from the HADS questionnaire, which is only validated in hospital inpatients and thus of limited applicability in an outpatient setting, similar results were found in large scale studies using validated questionnaires. Available evidence suggested that CNS tumour survivors had reduced social functioning[256,267], increased psychological distress[263] and poorer psychosexual development[284] as well as globally poorer quality of life scores[261]

than survivors of other cancers. Amongst non-CNS tumour survivors, sarcoma survivors appeared to have particularly poor psychological outcomes[261,284].

2.3.1.1.3 Physical Health

The impact of ongoing poor physical health on mental health was explored in a number of studies. Perhaps unsurprisingly, survivors with more marked disability, chronic ill health and physical sequalae of cancer treatment reported more adverse mental health outcomes. Lack of health insurance and inability to work due to disability were likely to have accounted for some of these effects. Issues with health insurance are less applicable to a UK population, but unemployment due to ill health is a global issue. Issues identified included problems with body image[161,257,278], generally increased prevalence of distress and poor mental health[157,286,288], increased risk of PTSD[244] and increased risk of suicidal ideation[259,290]. Whilst many of these results came from studies looking solely at survivors of CNS tumours or sarcoma, the increased prevalence of physical ill health in survivors of these conditions means that this was probably a reasonable sample group. There were also some more specific findings noted, such as obesity being associated with higher risk of depression in patients treated with BMT[273] and fatigue and sleep problems being associated with higher levels of anxiety, depression and somatisation[264], although these were only looked at in single studies.

2.3.1.1.4 Demographic Factors

Different demographic factors were found to impact on risk of mental ill health in a number of studies. Female survivors appeared to have greater risk of mental health difficulties than males[264,273,278,285,306]. PTSD in particular was more common in female cancer survivors[245].

A large scale study covering a diverse ethnic population found that, after adjustment for socioeconomic status, black survivors were less likely to report adverse mental health than white or Hispanic survivors[260], although no non-cancer controls were used in this study. No studies were found which reported on South Asian ethnicity. This probably reflects the fact that the majority of studies came from North America, where black and Hispanic individuals are the main minority ethnic groups, rather than the UK, where South Asian ethnicity is more common.

Another large-scale study found that survivors without siblings were at higher risk of psychological distress than survivors with siblings, whilst immigrants were at higher risk of distress than those who had not immigrated[285].

Smaller studies of specific tumour survivors also found poor social support, reduced disease acceptance, exposure to other stressful life events and a more emotion-oriented coping strategy were associated with higher levels of distress[287,300] and a larger study of whole families found reduced family functioning to be associated with increased risk of PTSD[276].

2.3.1.2 Alternative Viewpoints

Not all studies reported increased mental health problems, with some suggesting psychiatric disorder[258], work and educational attainment[283], poor body image and displeasure with current status[246] were no more common in CYP's cancer survivors. Anxiety and depression[256,277,278] and sleep problems[264] were no more prevalent in some cohorts of CYP's cancer survivors than controls. Some studies of CYP's cancer survivors found overall low levels of PTSD[305], depression[255,271] and other mental health problems[296], however lack of a control group makes it difficult to know whether these results simply reflect a lower prevalence of these disorders in the population sampled. One study found no evidence of depression in their cohort[255]. However, one of these studies looked only at survivors of TYA cancer and excluded survivors of childhood cancers and these studies tended to be smaller than those which did find increased risk of mental health disorder[256,277,278,283,296].

There was also some discrepancy in risk factors, with one study suggesting mental health difficulties were less common amongst individuals who had received cranial radiotherapy[306], although this was a very small and now dated study.

2.3.1.2.1 Positive Mental Health Outcomes

As well as reports of considerable difficulties, positive outcomes were also identified, with CYP's cancer survivors less likely to drink alcohol heavily or in a risky fashion than the general population[282], although this may reflect individuals following recommended lifestyle advice to minimise the risk of other late effects. Alternatively, the use of self-report may mean that these reported outcomes were not accurate, as individuals may not want to admit to behaving

in what is perceived to be an unhealthy way. Reduced risk of mental health problems[272] and behavioural problems were found in several very small studies[274,299] These findings were replicated in 2 larger scale studies[268,305] although use of sibling control groups limits the reliability of these findings, as siblings are known to suffer from their own mental health problems by virtue of being the sibling of someone with cancer[309]. It is only by comparing CYP's cancer survivors with a population unaffected by cancer that the true impact of cancer can be measured.

2.3.1.3 The Impact of Mental Health on Physical Health

Several very large cohort studies reported on the links between poor mental health and later physical health. We found evidence of links between poor psychological functioning and later risky health behaviours[277], such as increased heavy and risky drinking in survivors with depression and anxiety[173]. All-cause mortality was higher in survivors who had a history of suicidal ideation[259].

2.4 Discussion

This systematic review highlights the wide variety of psychological, psychiatric and psychosocial difficulties which may be faced by long term survivors of CYP's cancer. The high prevalence of these conditions means that all healthcare providers looking after these patients should be competent in identification of these problems.

Some potential causative and associated factors were also noted.

The increased risk of psychological distress seen in patients who had undergone cranial irradiation[244,290,298,308] and any form of brain surgery[275] may go some way to explaining why brain tumour survivors have greater mental health difficulties than survivors of other cancers. However, these patients also had lower average IQ[256] and increased physical health[275] problems which may also account for at least some of the differences seen.

Higher risk of mental health problems in patients treated with anthracyclines[161] may be due to the severe LEs often seen in these patients, particularly cardiomyopathy and congestive cardiac failure[310], and the association between chronic illness and poor mental health[286]. The anthracycline dose associated

with increased risk of cardiotoxicity (>300mg/m^2) is the same as the dose associated with increased mental distress[310], which adds further weight to this theory.

Patients with sarcoma are often treated with high dose anthracyclines[311,312], and it may be that the link between anthracycline treatment and increased distress is responsible for the increased mental health difficulties in sarcoma survivors. Additionally, these patients may have experienced disfiguring surgery which can cause marked distress[313].

The complex nature of cancer biology and treatment means that it is difficult to attribute psychiatric morbidity to a single cause. In the case of CNS tumours, for example, the currently available literature does not provide sufficient evidence on causation and it is not possible to determine how much morbidity is due to the direct effects of brain surgery and/or cranial radiotherapy and how much is due to residual disability.

Some studies had seemingly conflicting findings, for example a study finding increased interpersonal difficulties but no difference in work or educational attainment[283]. There may be many reasons for this, but it is possible that, as a result of having to continue with education during treatment, survivors are used to persisting with work or study despite ongoing difficulties. However, whilst it is positive to find good function in patients despite their difficulties, reduction of distress remains an important goal.

There were a number of limitations to the studies found. Many used siblings of survivors as a control group. Siblings will have similar genetics and upbringings to survivors and therefore allow good control for some confounding variables, however siblings have been shown to be at risk of considerable psychological distress themselves[309]. These studies therefore risk underestimating any increased prevalence of problems in survivors. Several of the studies finding no difference between prevalence of mental health problems in survivors versus controls used sibling controls and this may be the reason for the lack of difference found[160,256,270]. Some studies reporting low levels of mental health problems had no control group at all[274,297], making interpretation of these results even more difficult.

Most of the data from included studies was obtained from self-reports and questionnaires rather than clinician-made diagnoses. Self-reporting of symptoms is known to have a low predictive value for psychiatric diagnoses such as depression[158] and even well validated scores are less accurate in the presence of co-morbidity[159].

Reports of secondary care contacts are helpful, however these also risk seriously underestimating the prevalence of mental health problems, which are largely treated in a primary care setting[163].

Studies looking at antidepressant prescribing[156,265] did not provide information on the indication for prescription. Various antidepressants, including tricyclics and selective serotonin reuptake inhibitors (SSRIs), have been used to treat neuropathic pain[167]. Pain is another commonly reported symptom in cancer survivors[168] and therefore without data on indication for prescriptions of antidepressant medication, it is difficult to know how much increased prescribing is actually a result of increased prevalence of depression. Furthermore, antidepressant medications, in particular SSRIs, are also used for a number of psychiatric conditions, such as obsessive-compulsive disorder (OCD)[169], generalised anxiety disorder (GAD)[170] and bulimia nervosa[171], so whilst increased prescribing does likely indicate higher rates of psychiatric illness in this cohort, it would be useful to know specifically which conditions were more prevalent. In the United Kingdom, first line therapy for mild to moderate depression is psychological therapy such as cognitive behavioural therapy[166]. It is therefore likely that looking at antidepressant prescribing alone would underestimate the prevalence of depression in our population. Additionally, other studies looking at prescriptions of psychotropic medications[258] included analgesics. As increased rates of pain are seen in this population and therefore higher levels of analgesic prescribing would be expected cancer survivors[168], these studies do not accurately help to ascertain prevalence of mental health problems.

We found no studies reporting on primary-care-diagnosed mental health problems, despite the evidence that this is the commonest place for them to be diagnosed and managed[163]. Although the studies we found reporting on

prescribing data[156,265] did include prescriptions from primary care, diagnoses were not ascertained in these cases.

One study did report that cancer survivors were more likely to seek help for mental ill health than sibling controls[160], and it is therefore possible that some of the studies reporting increased mental health contacts amongst CYP cancer survivors are in part explained by an increase in help-seeking. However, papers which actually reported on clinician-made diagnoses or mental health problems[162,254,269,270], or prescriptions of psychotropic medications[156,165,258,265] accounted for a minority of included studies. It is unlikely that help-seeking would impact on self-reported or questionnaire-diagnosed problems, and thus increased help-seeking is not an adequate explanation for the overall increase in reported mental health problems amongst CYP cancer survivors.

Many studies included mostly survivors of ALL; although this is reflective of survivorship patterns, it may be that because these patients are at lower risk of problems, issues seen in survivors of rarer malignancies, such as poor body image[257], were not present at a statistically significant level. Even in studies where there were overall no difference in prevalence of problems, there were some sub-groups with increased risk of anxiety and depression[298] and sleep problems[264].

The studies included in this review focussed mainly on survivors of childhood cancer. Of 67 included studies, only 5 either included only TYA survivors or reported results for TYA survivors separately to childhood survivors[240,255,270,278,296]. Many other studies chose their age range such that the majority of TYA would have been included (many included under 18s or under 21s), however these studies did not report separately on TYA outcomes. Additionally, we found no studies including young adults up to the age of 30. This highlights the striking lack of literature on TYA survivors, who have historically been excluded from many trials[314].

Although this review included 67 studies, only 2 were carried out within the United Kingdom. Over half of the studies (n=35) were from North America. 26 were from mainland Europe, with 13 of these from Scandinavia, and the final 4 were from East Asia. Differences in the way healthcare is accessed, funded and paid for may well impact of the prevalence of diagnosed mental health

problems and there is therefore a need for more local work to ascertain the true prevalence of these debilitating issues in our population.

Whilst this systematic review identified a large number of papers, the broad definition of “mental health” means that there were likely some papers on specific conditions which were not identified. Further reviews considering specific mental health conditions may be useful in ascertaining the state of knowledge regarding particular diagnoses. Additionally, it was out with the scope of this review to look at intervention or treatment. A review of treatment options may enable the development of a clinical guideline which would assist clinicians caring for long term survivors of CYP cancer.

2.5 Conclusion

This systematic review has served to identify the wide range of mental health conditions experienced by survivors of CYP’s cancer. It is difficult to tease out the exact incidence, prevalence and risk-factors for their development from the existing literature. Given the potential for marked distress as a result of these conditions, further work is essential. Comprehensive linkage of primary care/community health and hospital records may help to resolve this and support robust identification of those diagnosed with cancer at a young age who are at risk of developing late mental health morbidity.

2.6 Repeat Literature Search

The initial literature search for this review was carried out some time ago. Therefore, in January 2020, the search was repeated to identify any important papers which had been published in the period between the initial search and the preparation of this thesis.

There were no papers published in the interim which altered the overall conclusions of the initial review, however, there were several papers published which further highlighted the need for more research in this area.

A moderate-sized American study highlighted the increased healthcare service utilisation of childhood cancer survivors with PTSD[315]. A small French study found increased anxiety and depression amongst childhood cancer survivors, although unlike the other study included in this review[172], they also found

increased risk of substance use[316]. They also reported lower risk of suicide[316], which is also in contrast to other studies[259,290]. A large German study reported increased mental distress amongst childhood cancer survivors, including suicidality, and highlighted females, those with lower educational levels, those with low incomes and unemployed individuals as at highest risk[317]. A moderate-sized Canadian study of ALL survivors found moderate prevalence of anxiety, depression and distress, which appeared higher in adolescent survivors than adult survivors, although the study lacked a control group[318]. A large study of neuroblastoma survivors found increased mental health difficulties, which were significantly more likely in those with chronic physical ill health, although this study was limited by the use of a sibling control group[319]. All of these studies were limited by self-report or questionnaire-based methodologies.

A systematic review and meta-analysis looking specifically at mental health in survivors of adolescent and young adult cancer highlighted the increased risk of mental ill health in this group, particularly amongst female survivors and those individuals who were older (within the “young adult” group) at the time of diagnosis[320]. Importantly, this review only included 4 papers and they highlight the important point that literature focussing on young adults is lacking[320]. A literature review which also focussed on survivors of adolescent and young adult cancer highlighted PTSD as a particular problem faced by this group[321].

A large Canadian study found increased rates of mental health services use amongst CYP’s cancer survivors compared to the general population, with survivors of adolescent cancer at greatest risk[322]. Unlike other studies, this work used administrative data to determine rates of hospital and other healthcare provider visits for mental health care. The main limitation of this work is that although almost all individuals diagnosed with cancer under the age of 15 were included, only about half of those aged 15-18 at diagnosis were included, and the work did not include any individuals diagnosed over the age of 18[322].

These further studies highlight the likely increased risk of mental ill health amongst survivors of CYP’s cancer. A single population-based study which used routinely-collected data was identified[322], however this was not based in the UK and thus similar work in a more local population remains necessary.

Chapter 3 Data Sources and Methods

3.1 The Yorkshire Specialist Register of Cancer in Children and Young People

The YSRCCYP is a regional, population-based register of cancer diagnoses and diagnoses of benign CNS tumours in children and young people in the North of England. The YSRCCYP covers the Yorkshire and the Humber Strategic Health Authority, which covers 15,000 square kilometres and has a population of 5 million[67]. The area covered by the YSRCCYP is show in figure 3a.

Figure 3a: Strategic Health Authorities in England, with Yorkshire and the Humber indicated by the arrow, in light blue[b]

[b] Image adapted from https://tableaumapping.wordpress.com/2013/07/16/uk-strategic-health-authorities/

Since 1974, data have been collected on all cases of cancer and non-malignant CNS tumours diagnosed in children aged 15 years and under living in the former Yorkshire Regional Health Authority[323]. Additionally, data have been collected on young people aged 15-29 years at the time of cancer/CNS tumour diagnosis since 1990. The YSRCCYP contains detailed information regarding socio-demographic factors, diagnoses and treatments, as well as information on tumour type (by both ICCC and Birch classifications), survival and relapse[323]. A list of all fields recorded in the YSRCCYP is attached in Appendix A. The majority of primary notification data is obtained directly from hospital records as either electronic downloads or manual abstractions, however where additional data sources have been used, these are described below. Vital status is checked 2-yearly, with pro-formas sent to hospital or primary care doctors to request this information. Deaths are then checked with the National Cancer Registration and Analysis Service (NCRAS).

3.1.1 Ethnicity

Where ethnicity information was available from hospital records, this was used as the primary method of classification. However, this field was occasionally incomplete, with no ethnicity available in around 10% of cases[324]. Onomap software, which calculates probabilities of patients being from different ethnic backgrounds based on their name[325], was therefore used to ascertain likely ethnicities for those where this information was not available from hospital records. Previous work on ethnicity using the YSRCCYP has shown very high levels of agreement between ethnic group classification from hospital records and those from Onomap[324]. In cases of discrepancies between ethnicity ascertained from hospital records and Onomap, the hospital records were assumed to be correct. Due to small numbers of individuals being from some ethnic groups, which makes meaningful analysis difficult, individuals were grouped into larger groups - White, South Asian or Other - for the purposes of analysis. The “South Asian” group consisted of those of Indian, Pakistani and Bangladeshi origins, the “White” group consisted of those of White British, White Irish and Other White Background and the “Other” group consisted of all other ethnicities, e.g. Black African, Black Caribbean, Other Asian, as well as mixed or unknown ethnicities. South Asian is the most common ethnic minority

in the UK, comprising just over 5% of the population in the 2011 National Census[326]. Use of Onomap reduced the number of records without a known ethnicity to 0.4%[324].

3.1.2 Deprivation

Deprivation was calculated using the Townsend deprivation index associated with the postcode where the patient lived at the time of their cancer diagnosis. The Townsend index uses Census data captured on unemployment, home ownership, vehicle ownership and household overcrowding to calculate a deprivation score for each Census output area and then aggregated up to electoral ward level[327]. This information was taken from the most recent national Census in 2011. For the purposes of this analysis, we grouped electoral ward areas into fifths, from 1 (least deprived) to 5 (most deprived).

The Townsend deprivation index has been used to assess deprivation on the YSRCCYP for many years, as it is a multi-modal assessment and takes into account factors other than household income[327]. It has also been available for longer than other measures, such as the Index of Multiple Deprivation, and is this more appropriate for a registry-based study going back to the 1970s.

3.2 Office for National Statistics

Mid-year estimates of the usual resident population for the 2011 census output areas within Yorkshire and the Humber were obtained from the Office for National Statistics (ONS)[328]. The number of individuals living in the Yorkshire and Humber region, which are estimated annually, were available for the years 2002-2017[328]. This information is broken down by age group and sex.

3.3 Hospital Episode Statistics

Hospital episode statistics (HES) are “a database containing details of all admissions, A and E attendances and outpatient appointments at NHS hospitals in England”[329]. These data are routinely collected by NHS services and maintained by NHS Digital (formerly the Health and Social Care Information Service; HSCIC)[329]. The primary purpose of HES data is to allow appropriate activity-based payment to NHS service providers, however the data can be made available for research purposes[329] and linked to cancer

registration data using personal identifiers such as NHS number. There have been concerns regarding the reliability of HES data, but steps over time have been to engage clinicians in the coding and collection of data, resulting in more reliable data from more recent years[330,331].

3.3.1 Mental Health Datasets

The HES data of most interest for the purposes of this thesis was that pertaining to mental health. Between 2006 and August 2014, data were collected in a dataset known as the Mental Health Minimum Dataset (MHMDS), which included information on contacts with adult inpatient, outpatient, community and mental health services[332]. In September 2014, in the dataset was renamed the Mental Health and Learning Disabilities Dataset (MHLDDS), and was expanded to include contacts with learning disability services as well as the mental health services collected by the MHMDS[333]. In February 2016, the dataset was renamed the Mental Health Services Dataset (MHSDS), and was extended to include contacts with autism services and services specifically for children and young people[334]. The MHMDS and MHLDDS include contacts by children and young people to general adult services, but does not include information on contacts with mental health, learning disability or autism services specifically for children and young people, as these data were only collected following the creation of the MHSDS[334].

This thesis used data from the MHMDS and MHLDDS but not MHSDS, because linked HES data were only available up to 2015. The focus of this thesis was on whether or not an individual had any recorded contact on the MHMDS or MHLDDS, due to the other data fields being poorly filled in. For example, “year of first known psychiatric contact” was provided in less than 30% of cases.

A list of all fields available from the provided HES mental health datasets is attached in Appendix B.

3.3.2 Hospital Admitted Patient Care Activity Dataset

The HES Hospital Admitted Patient Care Activity dataset contains details of all patients admitted to hospital for any reason, including dates of admission, diagnoses and any surgical operations or procedures. This information has been collected since 1998[335]. Throughout this thesis, this dataset will be

referred to as the “inpatient dataset”. Data were available for use in this thesis from 1998-2015. This dataset was used to identify individuals who had a listed mental health diagnosis. For the purposes of this work, mental health diagnoses included were the following ICD-10 codes:

- F10-F19: Mental and behavioural disorders due to psychoactive substance use
- F20-F29: Schizophrenia, schizotypal and delusional disorders
- F30-F39: Mood [affective] disorders
- F40-F48: Neurotic, stress-related and somatoform disorders
- F50: Eating disorders
- F60-F63; F65; F68-F69: Disorders of adult personality and behaviour (specifically excluding F64: Gender identity disorders and F66: Psychological and behavioural disorders associated with sexual development and orientation)
- F90-F93: Hyperkinetic disorders, conduct disorders, mixed disorders of conduct and emotions, and emotional disorders with onset specific to childhood
- F99: Unspecified mental disorder

For the purposes of this thesis, individuals were only considered to have had a mental health diagnosis on this dataset if this was recorded subsequent to their cancer diagnosis.

3.3.3 Combined Indicator of Mental Ill Health

Although not a specific HES dataset, the author then created a “combined indicator of mental ill health”. This consisted of individuals who had either a record on a mental health dataset (MHMDS or MHLDDS), a mental health diagnosis recorded on inpatient HES or both.

Individuals who received specialist mental health care between 2006 and 2015 will appear on the mental health dataset. Those who received specialist mental health care, but only on dates out-with this period, will not appear on the dataset. Individuals who had a hospital admission for a mental health disorder between 2006 and 2015 should appear on the mental health dataset and also have a mental health diagnosis on inpatient HES. Individuals who had a hospital admission for a mental health disorder before 2006, but since 1998, should have a mental health diagnosis recorded on inpatient HES. Individuals who accessed purely outpatient-based mental health services between 2006 and 2015 will have a record on mental health HES, but will only have a mental

health diagnosis recorded on inpatient HES if they were admitted to hospital for another reason and their mental health condition was listed as a co-morbidity. Individuals who had a mental health condition which was only ever managed by their GP will not appear on mental health HES, but may have a mental health diagnosis recorded on inpatient HES if they were admitted to hospital for another reason between 1998 and 2015, and their mental health condition was listed as a co-morbidity.

3.4 Leeds Teaching Hospitals NHS Trust Records

Leeds Teaching Hospitals NHS Trust (LTHT) is a large hospital trust located in Yorkshire. It provides care to both the local population in Leeds, as well as specialist services to the wider Yorkshire region[336].

For patients treated within LTHT, medical records were able to be directly accessed to obtain information about clinic attendances and follow-up appointments.

Electronic patient records on the PPM+ system (the system used by LTHT) contain details of clinic appointments, correspondence and investigations for the majority of clinical specialties, including oncology and haematology, for patients of all ages. Full electronic records were only accessible for those patients who had been treated in Leeds Teaching Hospitals NHS Trust.

In order to comply with licensing regulations from the Human Fertilisation and Embryology Authority (HFEA), data regarding use of fertility services is still kept in paper records.

3.5 Leeds Fertility

Our local assisted conception unit, Leeds Fertility, were able to provide a list of all patients who had undergone semen cryopreservation since 2008. Their indication for banking was also recorded, which meant it was possible to identify all patients who had undergone semen cryopreservation because of a diagnosis of malignant disease.

A retrospective case note review of the paper fertility service notes was carried out in order to identify the following characteristics:

- Age at banking

- Paternity status at time of banking

- Semen analysis at banking

- Whether or not the patient had been followed up by fertility services after banking

- Whether or not a post-treatment semen analysis had taken place and, if so, whether post-treatment semen analysis was normal.

3.6 Methodology

3.6.1 Cohort Selection

Details of cancer diagnoses were obtained from the YSRCCYP. Eligible individuals were diagnosed with a malignancy or non-malignant brain tumour between 1974 and 2012, before their 30th birthday, within the Yorkshire and Humber region, and had survived a minimum of 5 years post diagnosis. Data were extracted from the YSRCCYP in June 2017. Data were available on 9609 individuals, of whom 7253 (75.5%) had survived for at least 5 years following an initial cancer diagnosis. These 7253 individuals made up the cancer survivor cohort described in this thesis. Further details of this cohort, including their characteristics and how they differ from those individuals who did not become 5 year survivors, are given in Chapter 4: Cohort Description.

3.6.2 Data linkage

NHS Digital were provided with a list of all patients on the YSRCCYP through a secure file transfer process (FTP) and returned details of contacts recorded on the MHMDS and MHLDDS between 2006 and 2015, as well as contacts on the inpatient dataset since 1998. Data linkage and extraction was performed by NHS Digital using the following identifiers from the YSRCCYP: NHS number, date of birth, sex and postcode.

Any individual with a linked record on the MHMDS or MHLDDS was considered to have accessed specialist mental health services.

The inpatient HES data were also searched for any admissions where a mental health condition was either the primary reason for admission or a listed co-morbidity. The ICD diagnostic codes included as “mental health conditions” are

listed earlier in this chapter, under section 1.3.2 Hospital Admitted Patient Care Activity Dataset. Individuals who had an admission primarily for a mental health condition were also considered to have accessed specialist mental health services, whilst those individuals who had a mental health condition listed as a co-morbidity were considered to have a mental health diagnosis.

3.6.3 Yorkshire Population Data

NHS Digital also provided tabulations of the number of contacts recorded on the MHMDS and MHLDDS between 2006 and 2015 for individuals living in Yorkshire and The Humber. Although it was not possible to obtain individual-level records, aggregated data tables were available, with number of contacts broken down by 5-year age group and sex.

Inpatient HES data was also obtained for all individuals in Yorkshire and The Humber, and, like the inpatient HES data for the YSRCCYP population, were searched for admissions with a documented mental health condition as a reason for admission or a co-morbidity.

The number of contacts on the MHMDS and MHLDDS were compared to the estimated population from the ONS in order to generate a rate of specialist mental health care access in the population of Yorkshire.

Rates of documented mental health conditions on inpatient HES were also compared to the estimated population from the ONS in order to generate a rate of documented mental health conditions in the Yorkshire population.

3.6.4 Fertility Data

Data on semen cryopreservation, provided by Leeds Fertility, were linked to the survivor cohort from the YSRCCYP to identify patients who were both 5 year survivors of CYP's cancer and who had undergone semen cryopreservation.

Patients on the YSRCCYP who were male diagnosed with cancer in 2008 or later and who were 13 or older at the time of diagnosis were identified as controls. As there are multiple potential fertility services within the Yorkshire area, only patients who were likely to have stored semen at Leeds Fertility (those from Bradford, Wakefield, Airedale, Harrogate, Leeds, Halifax, Huddersfield and Harrogate) were included as controls. Data on cancer

diagnosis as well as their age at diagnosis and year of diagnosis, were ascertained directly from the YSRCCYP.

3.7 Statistical Methods

3.7.1 Standardised Incidence Ratios

Standardised incidence ratios were calculated to compare the incidence of contacts with specialist mental health services (based only on the presence of a linked record on the MHMDS or MHLDDS) between 5 year survivors of CYP's cancer with a record on the YSRCCYP and the Yorkshire population as a whole. This calculation was made using the "PHE tool for calculating common public health statistics and confidence intervals", downloaded from the PHE Fingertips website[337].

3.7.2 Regression

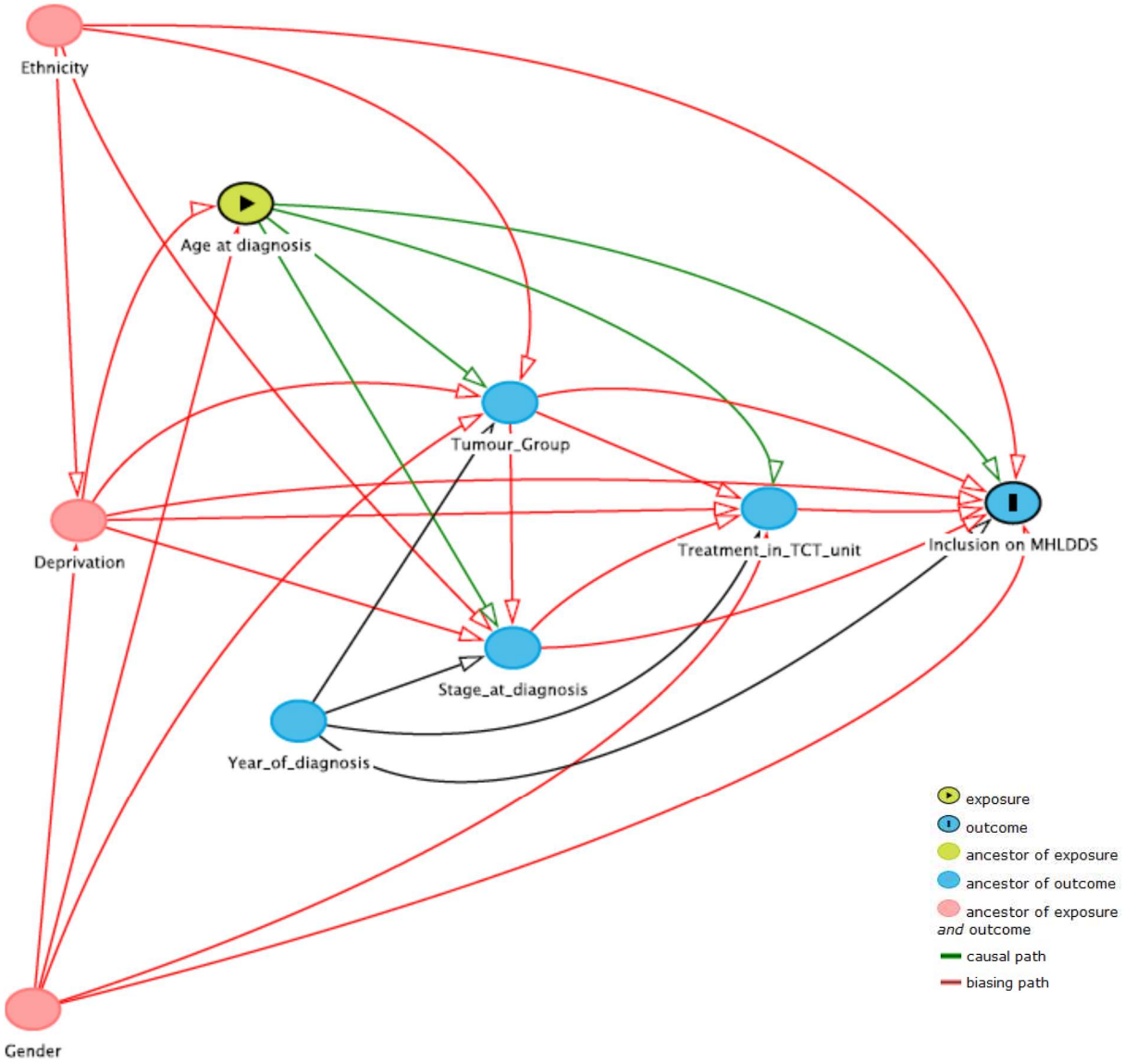
Logistic regression was performed to determine the odds ratio (and 95% confidence intervals) of having at least one contact with specialist mental health services (identified by the presence of a linked record on the MHMDS or MHLDDS, or a record on inpatient HES where a mental health diagnosis was the primary reason for admission), and of having at least one mental health co-morbidity (identified by a record on inpatient HES where a mental health diagnosis was a listed co-morbidity) for different exposures, including disease-related factors such as tumour type and stage at diagnosis, as well as demographic factors such as age at diagnosis, race and deprivation status. All statistical analyses were performed using Stata-15 software.

3.7.3 Causal Inference Methods

Causal inference methods were used to identify an appropriate minimal set of confounders for each risk factor of interest, with separate regression models run for each variable[338]. Causal inference methods and directed acyclic graphs (DAGs), were chosen as they provide a robust way of identifying confounding variables and causal pathways whilst reducing the risk of over adjustment[339] and increasing statistical efficiency[340], and are thus preferable to other statistical methods[341]. Causal inference methodology has been shown to be effective in clinical research[342]. DAGs were created to define the theoretical causal relationships with mental ill health using DAGitty software[343] (figure 3.1).

DAGs with each possible primary risk factor of interest are provided in Appendix C.

Figure 3.1 A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and "age at diagnosis" highlighted as the primary risk factor of interest (exposure), together with all other variables.



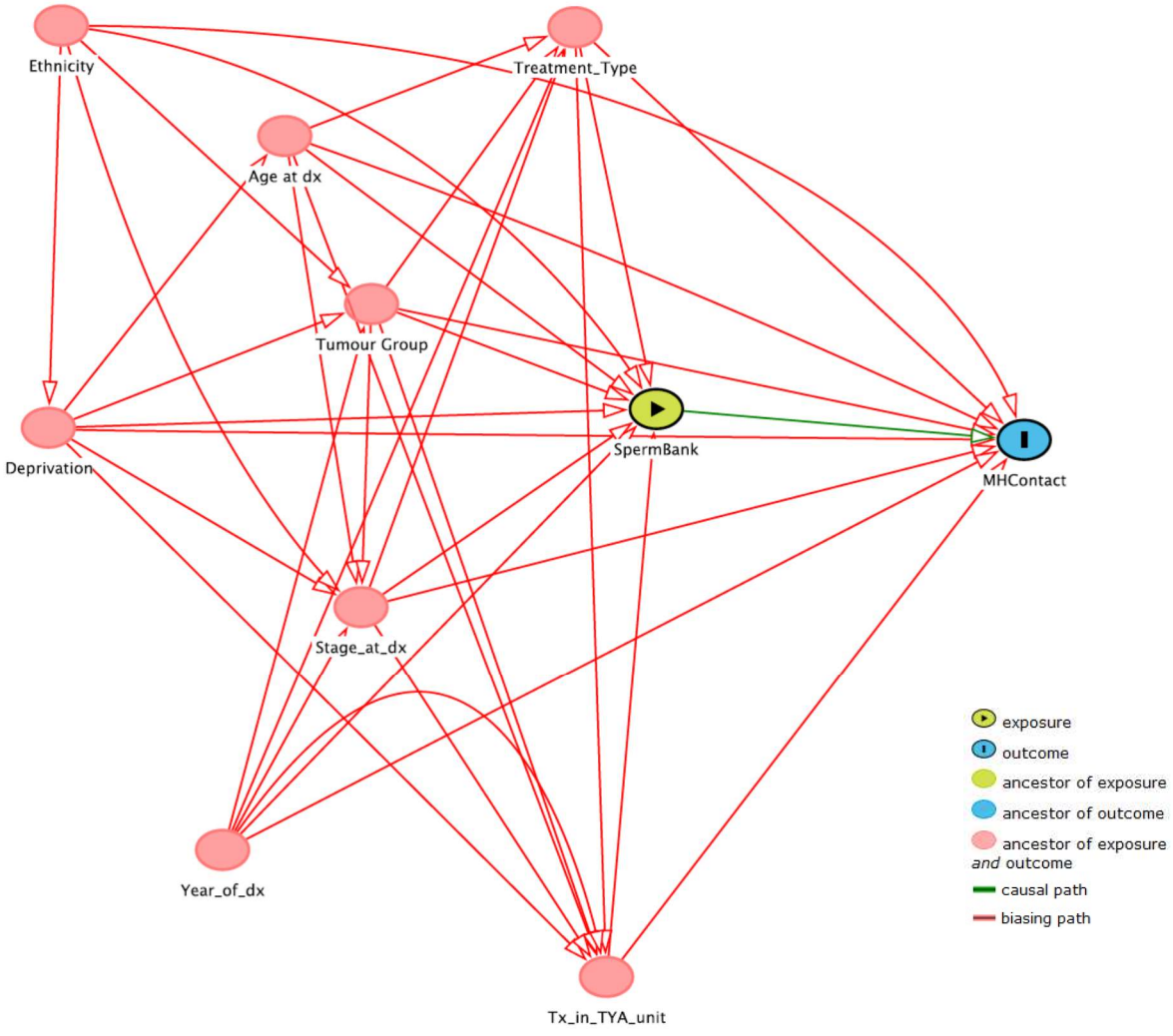
DAGitty software suggested the following minimal adjustment sets for each primary risk factor (exposure):

- Age at diagnosis – deprivation, gender
- Deprivation – ethnicity, gender

- Ethnicity – nil (ethnicity sufficient on its own)
- Gender – nil (gender sufficient on its own)
- Stage at diagnosis – age at diagnosis, deprivation, ethnicity, tumour group, year of diagnosis
- Treatment at TYA unit – age at diagnosis, deprivation, gender, stage at diagnosis, tumour group, year of diagnosis
- Tumour group – age at diagnosis, deprivation, ethnicity, gender, year of diagnosis
- Year of diagnosis – nil (year sufficient on its own)

A further DAG was created specifically to look at the relationship between semen cryopreservation and mental ill health. Gender was removed from the causal pathway, given that only males would be offered semen banking, and semen cryopreservation was added in. This DAG is shown in figure 3.2.

Figure 3.2 A Directed Acyclic Graph describing the causal relationship between risk of mental health hospitalisation and sperm banking



DAGitty software suggested the following minimal adjustment set when looking at sperm banking as the primary risk factor: age at diagnosis, deprivation, ethnicity, stage at diagnosis, treatment type, tumour group, treatment at TYA unit, year of diagnosis.

3.7.4 χ^2 and Fisher's Exact Tests

In order to test the hypothesis that there was a difference between groups, such as total individuals on the YSRCCYP and 5 Year Survivors, χ^2 was used to generate p values, with $p<0.05$ being regarded as statistically significant. Where smaller numbers were present, such as in the fertility work in chapter 6, Fisher's exact test was used as an alternative.

3.8 Ethical Approval

The YSRCCYP has longstanding ethical approval from the Northern and Yorkshire Multi Centre Research Ethics Committee (reference MREC/0/1/3)[67], and approval from the Health Research Authority Confidentiality Advisory Group (reference 1-07(b)/2014). These approvals allow identifiable cancer registration data to be used without the need for explicit patient consent, although all individuals have the opportunity to opt out of the registry. Approvals also allow the linkage of registry data to other healthcare data sources. Specific, additional ethical approval was not required for the work described in this thesis to be carried out.

Chapter 4 Cohort Description

4.1 Yorkshire Specialist Register of Cancer in Children and Young People 5-plus year survivors

The YSRCCYP contained information on 7253 patients who had survived at least 5 years after a diagnosis of cancer and were aged under 30 years at diagnosis. Patients were diagnosed between 1974 and 2012; until 1990, all patients on the register were under 15 years old at diagnosis and since 1990 patients have been included if they were diagnosed before their 30th birthday. The decision to include patients up to the age of 30 was taken to ensure all in the TYA age group were included, and to try to broaden this group to include older patients who may still be considered “young adults”. The inclusion of patients up to the age of 40, consistent with some definitions of “adolescents and young adults” was not considered feasible from an administrative point of view. Data recorded included sex, age at diagnosis and diagnosis, classified according to the ICCC. Data on Townsend deprivation score (based on postcode at time of diagnosis), ethnicity, year of diagnosis and duration of follow up was also recorded. At the time of data extraction, 7092 (97.8%) individuals were alive. See Chapter 3: Data Sources and Methods for full details.

Of the 7253 5 year survivors, 59.8% (4335) were male. Median age at diagnosis was 15 years, interquartile range (IQR) 5-24 years. The most common malignant diagnoses were leukaemias (1458 cases, 20.1%), lymphomas (1421 cases, 19.6%) and central nervous system tumours (1279 cases, 17.6%). Patients had been followed up for a mean of 16.2 years (median length of follow up 15 years, IQR 9-22 years). As described in the introduction, Section 1.1.3: Cancer Classification, some cancers are most common in different age groups. Therefore, median age at diagnosis for individuals with a diagnosis within each of the ICCC diagnostic groups is shown in table 4.1. CNS tumours were separated into high and low grade tumours.

Table 4.1 Median age at cancer diagnosis in years for each International Classification of Childhood Cancer diagnostic group, with Central Nervous System tumours separated into high and low grade tumours.

Diagnostic Group	Median age at diagnosis (IQR), years
Leukaemias	6 (3-14)
Lymphomas	20 (13-25)
CNS Tumours	11 (5-20)
Neuroblastoma	1 (0-4)
Retinoblastoma	1 (0-2)
Renal	3 (1-7)
Hepatic	1 (3-18.5)
Bone	14 (11-20)
Soft Tissue	14 (5-24)
Germ Cell	24 (19-27)
Other Epithelial	24 (19-27.5)
Other	23 (12-29)
All Diagnostic Groups	15 (5-24)

Characteristics of eligible patients on the register are summarised in table 4.2. The criteria for being an “eligible” patient is described in Chapter 3: Data Sources and Methods, Section 3.1: The Yorkshire Specialist Register of Cancer in Children and Young People. Note that period of diagnosis is categorised in 5 year brackets, aside from the earliest period (1974-1979; 6 years) and the latest period (2010-2012; 3 years). This was to enable the periods before and after 1990, when patients aged 15-29 years at diagnosis started to be included on the register, to be clearly identifiable, whilst breaking down the majority of years of diagnosis into equal groups. All patients diagnosed before 1990 were under 15 at the time of diagnosis. This change in

recording also means that the majority of patients with longer follow up periods would have been diagnosed before their 15th birthday.

Table 4.2 Baseline characteristics of eligible patients and 5 year survivors identified from the Yorkshire Specialist Register of Cancer in Children and Young People

Characteristic	Eligible registry patients	5 year survivors	χ^2 statistic (p value)[c]
Gender			
Male	5618 (58.5%)	4335 (59.8%)	2.9
Female	3991 (41.5%)	2918 (40.2%)	(0.0866)
Age group at diagnosis			
0-4	2226 (23.2%)	1631 (22.5%)	38.7
5-9	1294 (13.5%)	916 (12.6%)	(<0.001)*
10-14	1030 (10.7%)	1002 (13.8%)	
15-19	1233 (12.8%)	883 (12.2%)	
20-24	1565 (16.3%)	1178 (16.2%)	
25-29	2261 (23.5%)	1643 (22.7%)	
Tumour Group (International Classification of Childhood Cancer[25])			
Leukaemia	1943 (20.2%)	1458 (20.1%)	143
Lymphoma	1734 (18.1%)	1421 (19.6%)	(<0.001)*
CNS	1765 (18.4%)	1279 (17.6%)	
Neuroblastoma	350 (3.6%)	229 (3.2%)	
Retinoblastoma	150 (1.6%)	124 (1.7%)	
Renal	314 (3.3%)	254 (3.5%)	

[c] * denotes statistical significance

Hepatic	84 (0.9%)	44 (0.6%)	
Bone	435 (4.5%)	301 (4.1%)	
Soft Tissue	579 (6.0%)	437 (6.0%)	
Germ Cell	1307 (13.6%)	1144 (15.8%)	
Other Epithelial	752 (7.8%)	548 (7.6%)	
Other	196 (2.0%)	14 (0.2%)	
Year of Diagnosis			
1974-1979	529 (5.5%)	403 (5.6%)	567
1980-1984	400 (4.2%)	327 (4.5%)	(<0.001)*
1985-1989	443 (4.6%)	386 (5.3%)	
1990-1994	1153 (12.0%)	1039 (14.3%)	
1995-1999	1284 (13.4%)	1179 (16.3%)	
2000-2004	1643 (17.1%)	1505 (20.8%)	
2005-2009	1754 (18.3%)	1641 (22.6%)	
2010-2012	2403 (25.0%)	773 (10.7%)	
Deprivation fifth (based on Townsend score of postcode at diagnosis)			
1 (least deprived)	1812 (18.9%)	1344 (18.5%)	1.2
2	1767 (18.4%)	1351 (18.6%)	(0.885)
3	1730 (18.7%)	1345 (18.5%)	
4	1792 (18.7%)	1357 (18.7%)	
5 (most deprived)	2488 (26.0%)	1856 (25.6%)	
Ethnic Group			
White	8180 (85.1%)	6474 (89.3%)	118
South Asian	666 (6.9%)	453 (6.3%)	(<0.001)*
Other	417 (4.3%)	242 (3.3%)	

Unknown	346 (3.6%)	84 (1.2%)	
Duration of Follow Up			
<10 years	3110 (32.3%)	2113 (29.1%)	91.2
10-19 years	3297 (34.3%)	2774 (38.2%)	(<0.001)*
20-29 years	2022 (21.0%)	1587 (21.9%)	
30-39 years	817 (8.5%)	669 (9.2%)	
40+ years	363 (3.8%)	130 (1.8%)	
Vital Status as of June 2017			
Alive	8541 (88.9%)	7092 (97.8%)	484
Dead	1068 (11.1%)	161 (2.2%)	(<0.001)*

Individuals who survived at least 5 years were very similar in gender and deprivation status to all individuals on the register. A greater proportion of individuals who had survived at least 5 years were of White ethnicity. This is in keeping with studies which report a survival advantage for White individuals over those from ethnic minorities[344], particularly in those with ALL[345], despite there being a higher risk of childhood cancer in ethnic minority populations[346]. This may be in part due to increased socio-economic deprivation amongst individuals from non-White groups[347]. There were differences in tumour types and age at diagnosis between individuals who had survived 5 years and all individuals on the register, which is unsurprising given the differences in prognosis between tumour types, and their peak onset at different ages.

NCSI risk levels[101] were available for patients who were currently under the long-term follow up service in LTHT. 1509 (20.8%) patients had an NCSI level recorded in the LTHT database who had also been identified as 5 year survivors from the YSRCCYP. These are summarised in table 4.3. Further details on the NCSI levels, their history, and how they are assigned, are described in the introduction, Section 1.5.1: Risk of Late Effects.

Table 4.3 Available National Cancer Survivorship Initiative levels for patients included in analysis

National Cancer Survivorship Initiative Level	5 year survivors
1	68 (4%)
2	1056 (66%)
3	476 (30%)

Of patients who had an NCSI level allocated, the majority (66%) were level 2, with just under one third allocated level 3. Only a very small number were level 1. Compared to other studies, the number of individuals with NCSI level 1 was very low[348]. This is likely to reflect the fact that, in line with national recommendations[99], many patients with NCSI level 1 are not followed up in clinic and thus information regarding their NCSI level was not available on our database of patients receiving active follow up.

There were some differences between those patients who had an allocated NCSI level and those who didn't. Patients without an assigned NCSI level were more likely to be older at the time of diagnosis (47.2% diagnosed after age 19 vs 7.4% of patients with an assigned NCSI level). Far more patients without an assigned NCSI had a diagnosis of germ cell tumour (17.7% vs 8.5%), which may be due to the fact that these patients often receive less intensive treatment, sometimes being treated with surgery only, and thus referral to long term follow up may not be necessary[99]. Patients who had an assigned NCSI level appeared to have been diagnosed earlier (39.6% diagnosed before 1990, compared to 9.0% of patients without an assigned NCSI level). This may reflect the fact that older treatments were often more toxic and that both cancer and survival were rarer at this time[21,22] meaning a higher percentage of patients were followed up. Additionally, some of the patients diagnosed more recently would still be under standard oncology follow up, as referral to long term follow up only takes place 5 years after the cessation of treatment. These differences are summarised in table 4.4.

Table 4.4 Characteristics of 5 year survivors with and without an allocated National Cancer Survivorship Initiative level.

Characteristic	NCSI level assigned No of patients	No NCSI level assigned No of patients	χ^2 statistic (p value)[d]
Gender			
Male	874 (57.9%)	3461 (60.3%)	2.71
Female	635 (42.1%)	2283 (39.7%)	0.100
Age group at diagnosis			
0-4	515 (34.1%)	1116 (19.4%)	962
5-9	345 (22.9%)	571 (9.9%)	(<0.001)*
10-14	386 (25.6%)	616 (10.7%)	
15-19	152 (10.1%)	731 (12.7%)	
20-24	68 (4.5%)	1110 (19.3%)	
25-29	43 (2.8%)	1600 (19.4%)	
Tumour Group (International Classification of Childhood Cancer[25])			
Leukaemia	514 (34.1%)	944 (16.4%)	407
Lymphoma	244 (16.2%)	1177 (20.5%)	(<0.001)*
CNS	238 (15.8%)	1041 (18.1%)	
Neuroblastoma	65 (4.3%)	164 (2.9%)	
Retinoblastoma	21 (1.4%)	103 (1.8%)	
Renal	81 (5.4%)	173 (3.0%)	
Hepatic	9 (0.6%)	35 (0.6%)	
Bone	88 (5.8%)	213 (3.7%)	

[d] *denotes statistical significance

Soft Tissue	100 (6.6%)	337 (5.9%)	
Germ Cell	129 (8.5%)	1015 (17.7%)	
Other Epithelial	20 (1.3%)	528 (9.2%)	
Other	0	14 (0.2%)	
Year of Diagnosis			
1974-1979	232 (15.4%)	171 (3.0%)	958
1980-1984	168 (11.1%)	159 (2.8%)	(<0.001)*
1985-1989	198 (13.1%)	188 (3.3%)	
1990-1994	208 (13.8%)	831 (14.5%)	
1995-1999	232 (15.4%)	947 (16.5%)	
2000-2004	246 (16.3%)	1259 (21.9%)	
2005-2009	184 (12.2%)	1457 (25.4%)	
2010-2012	41 (2.7%)	732 (12.7%)	
Deprivation fifth (based on Townsend score of postcode at diagnosis)			
1	298 (19.8%)	1046 (18.2%)	12.8
2	315 (20.9%)	1036 (18.0%)	(0.01)*
3	262 (17.4%)	1083 (18.9%)	
4	250 (16.6%)	1107 (19.3%)	
5	384 (25.5%)	1472 (25.6%)	
Ethnic Group			
White	1360 (90.1%)	5114 (89.0%)	27
South Asian	114 (7.6%)	339 (5.9%)	(<0.001)*
Other	30 (2.0%)	212 (3.7%)	
Unknown	5 (0.3%)	79 (1.4%)	
Duration of Follow Up			

<10 years	180 (11.9%)	1913 (33.3%)	789
10-19 years	477 (31.6%)	2297 (40.0%)	(<0.001)*
20-29 years	417 (27.6%)	1170 (20.4%)	
30-39 years	362 (24.0%)	307 (5.3%)	
40+ years	73 (4.8%)	57 (1.0%)	
Vital Status as of June 2017			
Alive	1495 (99.1%)	5597 (97.4%)	14.7
Dead	14 (0.9%)	147 (2.6%)	(<0.001)*

4.2 Yorkshire Population

The Yorkshire population was used as a comparison group throughout this thesis. Their baselines characteristics are summarised in table 4.5, obtained from the 2011 census data[349] and Mendeley data[350,351]. As at March 2011, Yorkshire had a population of 5.3 million people. Just over half (50.8%) were female. The median age at this time within Yorkshire was 39 years. The population were largely white (88.8%), with South Asians being a notable minority (6.0%). Slightly more individuals live in the most deprived areas than other areas (21.5% in quintile 5 compared to just over 19% in quintile 1-4). The data which were available regarding gender, age, ethnicity and deprivation distributions in Yorkshire are described in Table 4.5.

Table 4.5 Characteristics of the Yorkshire Population, based on the 2011 census

Characteristic	Yorkshire Population
Gender	
Male	2598078 (49.2%)
Female	2685655 (50.8%)
Age Group	
0-4	328447 (6.2%)

5-9	297475 (5.6%)
10-14	306096 (5.8%)
15-19	348645 (6.6%)
20-24	382679 (7.2%)
25-29	347304 (6.6%)
30-34	321328 (6.1%)
35 and over	2951759 (55.9%)
Ethnicity	
White	4691956 (88.8%)
South Asian	317568 (6.0%)
Other	274209 (5.2%)
Deprivation Fifth	
1	1030528 (19.5%)
2	1049472 (19.8%)
3	1046435 (19.8%)
4	1023789 (19.4%)
5	1137988 (21.5%)

4.3 Comparisons Between the Yorkshire Specialist Register of Cancer in Children and Young People Cohort and the Yorkshire Population

The Yorkshire population as a whole consisted of almost equal numbers of males and females, whilst there were many more males in the YSRCCYP 5 year survivor cohort. This likely reflects the fact that cancer in children, who have been included on the register for a much longer time period than TYAs, is more common in males[14]. The ethnic composition of the YSRCCYP 5 year survivor cohort was very similar to that of the Yorkshire population as a whole.

There were a greater proportion of individuals from the most deprived fifth on the YSRCCYP compared to Yorkshire as a whole. This is in keeping with previous literature, which suggests an increased risk of cancer in the most deprived groups[352], although this is not a consistent finding[353]. Some cancers affecting the young adult population, including breast[354] and colorectal[355] cancers, are also more common in more deprived populations, probably due to increased rates of smoking and obesity, and this may also account for some of the variation seen with deprivation.

Chapter 5 Mental Health Services Use and Co-Morbidity in 5 Year plus Survivors of Childhood and Young Adult Cancer

As described in the methods section, data linkage techniques allowed us to determine patients in our cohort of cancer survivors who had had at least one recorded episode on the MHMDS or MHLDDS, indicating contact with specialist mental health services, in the period 2006-2015. We were also able to determine patients who had had at least one recorded mental health diagnosis (either as the reason for admission or a documented co-morbidity) from inpatient HES records for the period 1998-2015.

This chapter describes which patients experienced a mental health episode, and whether any particular groups appeared at greater risk of having these records.

5.1 Characteristics of Childhood and Young Adult Cancer Survivors with Mental Health Services Contacts

In total, 777 (10.7%) survivors had at least one recorded episode on the MHMDS or MHLDDS, indicating contact with specialist mental health services in the period 2006-2015.

Characteristics of patients who had a recorded episode on the MHMDS and/or MHLDDS are summarised in table 5.1a. Data on ethnicity were available for 763 of the 777 patients. All other variables (age at diagnosis, cancer type, year of diagnosis, deprivation score) were available for all 777 patients. Median age at diagnosis in these patients was 19 years (interquartile range 10-25 years). Just over half were male. Most commonly seen diagnoses were germ cell tumours in males and non-CNS solid tumours in females. The majority of patients were White British. Age at diagnosis, diagnostic group, period of diagnosis, deprivation quintile and ethnic group for patients with a recorded episode on the MHMDS and/or MHLDDS are also shown in figures 5.1a-5.1e, respectively. A higher proportion of individuals diagnosed with cancer in the TYA period (15-29) had a recorded episode on the MHMDS and/or MHLDDS than those diagnosed in childhood (0-14). A higher proportion of females appeared to have a recorded episode on the MHMDS and/or MHLDDS than males, aside from in those aged 5-14 at diagnosis, where a higher proportion of

males had a recorded episode on the MHMDS and/or MHLDDS. A higher proportion of individuals with CNS tumours, lymphomas and germ cell tumours had a recorded episode on the MHMDS and/or MHLDDS than of individuals with leukaemias and non-CNS solid tumours. A higher proportion of individuals from the most deprived fifth of areas had a recorded episode on the MHMDS and/or MHLDDS than individuals from less deprived areas. A higher proportion of White British individuals had a recorded episode on the MHMDS and/or MHLDDS than individuals of other ethnicities. A higher proportion of individuals diagnosed with cancer between 2005 and 2009 had a recorded episode on the MHMDS and/or MHLDDS than individuals diagnosed in other periods. Section 5.6: Groups at Increased Risk of Mental Health Services Use and Co-Morbidity uses logistic regression to determine which of these differences are statistically significant.

Table 5.1a Characteristics of 5 year childhood and young adult cancer survivors who had a recorded specialist mental health contact[e]

Variable		Number with a recorded episode on MHMDS and/or MHLDDS (total individuals on registry)		Proportion of each group with a recorded episode on MHMDS and/or MHLDDS	
		Male	Female	Male	Female
Age Group at diagnosis (years)	0-4	49 (901)	60 (723)	5.4%	8.3%
	5-9	50 (526)	27 (390)	9.5%	6.9%
	10-14	58 (562)	39 (440)	10.3%	8.9%
	15-19	63 (519)	62 (364)	12.1%	17.0%
	20-24	95 (758)	64 (420)	12.5%	15.2%
	25-29	126 (1026)	84 (581)	12.3%	14.5%
Diagnostic group	Leukaemia	62 (833)	54 (621)	7.4%	8.7%
	Lymphoma	95 (857)	71 (563)	11.1%	12.6%

[e] CNS = Central Nervous System; non-CNS solid = all solid tumours out with the central nervous system, including lymphomas but excluding germ cell tumours

	CNS	85 (692)	76 (587)	12.3%	12.9%
	Germ cell	128 (1005)	13 (138)	12.7%	9.4%
	Non-CNS solid	71 (942)	122 (1004)	7.5%	12.1%
Period of diagnosis	1974-1979	18 (230)	11 (173)	7.8%	6.4%
	1980-1984	14 (181)	17 (146)	7.7%	11.6%
	1985-1989	18 (212)	29 (174)	8.5%	16.7%
	1990-1994	64 (622)	52 (417)	10.3%	12.5%
	1995-1999	80 (718)	49 (461)	11.1%	10.6%
	2000-2004	94 (911)	69 (594)	10.3%	11.6%
	2005-2009	123 (989)	84 (652)	12.4%	12.9%
	2010-2012	30 (472)	25 (301)	6.4%	8.3%
Deprivation category (based on Townsend deprivation index)	1 (least deprived)	58 (785)	57 (559)	7.4%	10.2%
	2	76 (824)	61 (527)	9.2%	11.6%

	3	76 (810)	59 (535)	9.4%	11.0%
	4	86 (828)	63 (529)	10.4%	11.9%
	5 (most deprived)	145 (1088)	96 (768)	13.3%	12.5%
Ethnicity	White British	394 (3798)	299 (2566)	10.4%	11.7%
	South Asian	26 (291)	21 (198)	8.9%	10.6%
	Other	12 (159)	11 (118)	7.5%	9.3%

Figure 5.1a Age at diagnosis for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded episode on the Mental Health Services Data Set and/or the Mental Health and Learning Disability Data Set

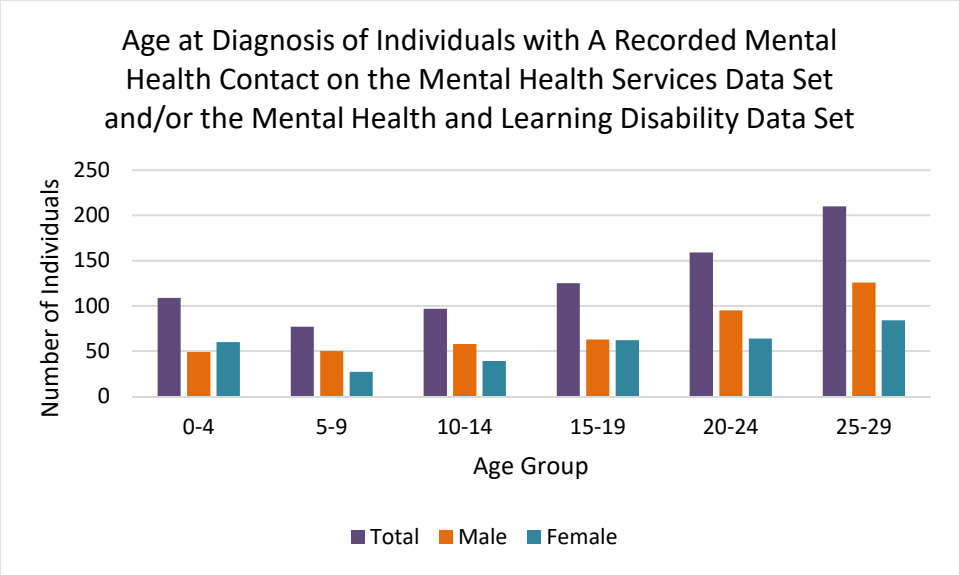


Figure 5.1b Diagnostic group for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded episode on the Mental Health Services Data Set and/or the Mental Health and Learning Disability Data Set

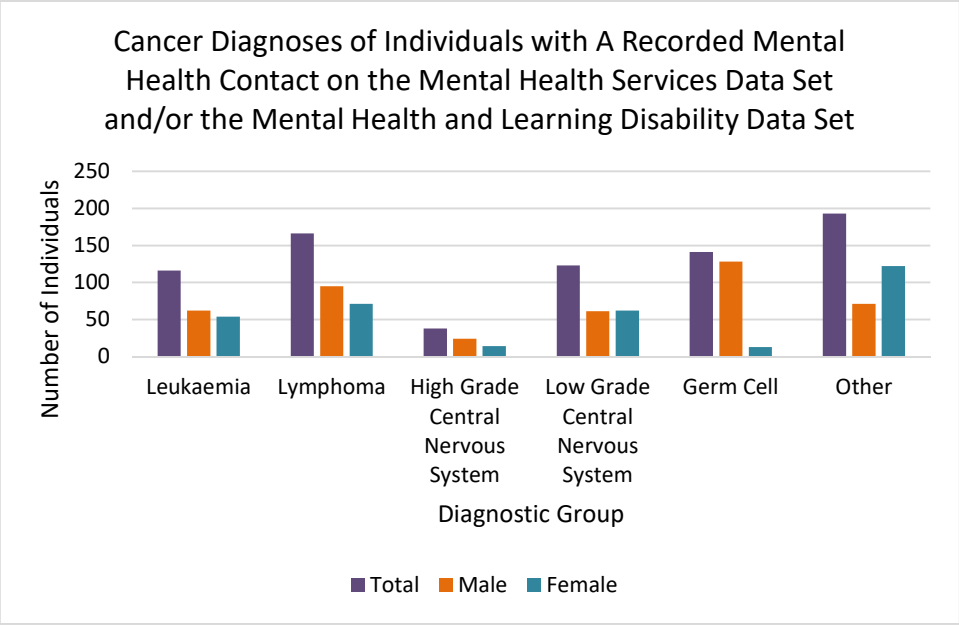


Figure 5.1c Period of diagnosis for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded episode on the Mental Health Services Data Set and/or the Mental Health and Learning Disability Data Set

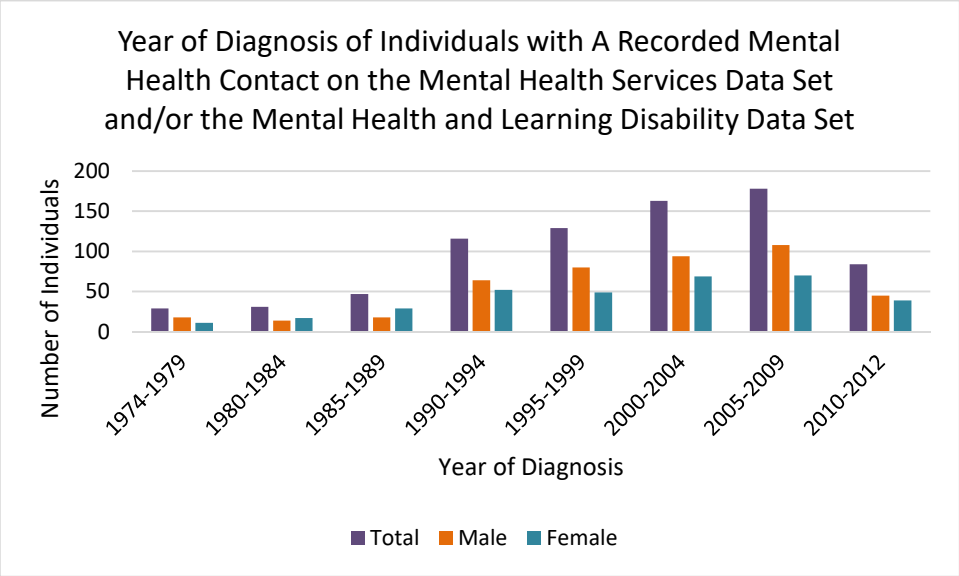


Figure 5.1d Deprivation quintile for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded episode on the Mental Health Services Data Set and/or the Mental Health and Learning Disability Data Set

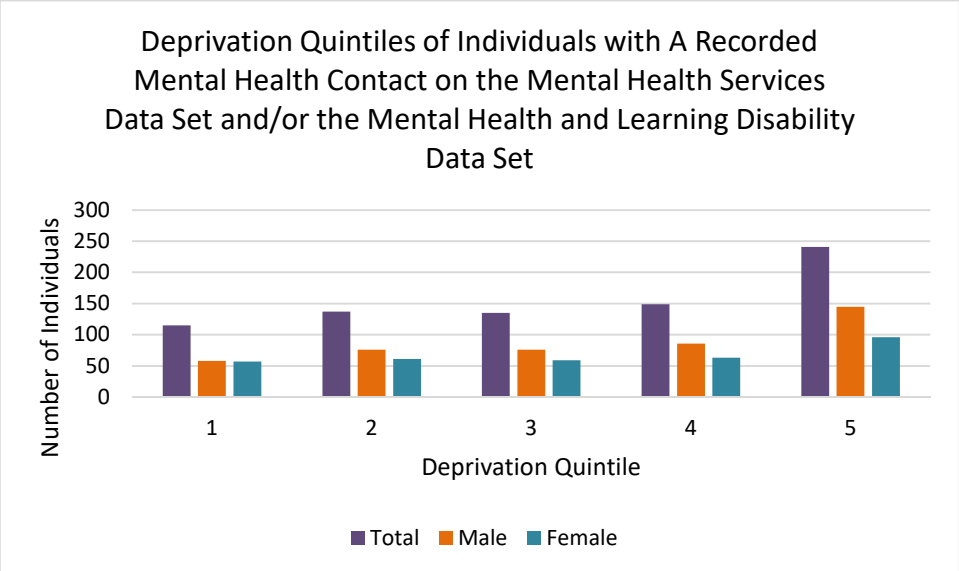
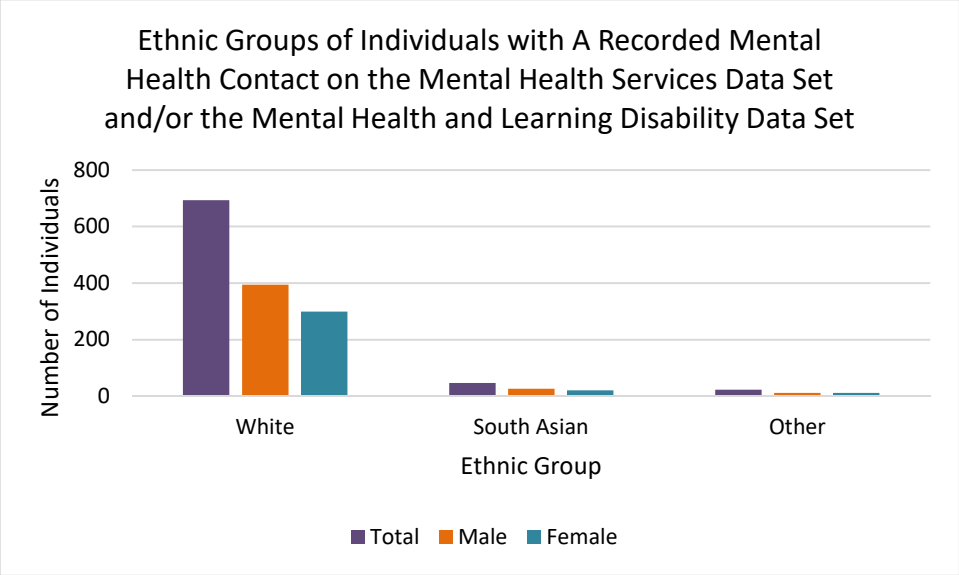


Figure 5.1e Ethnic group for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded episode on the Mental Health Services Data Set and/or the Mental Health and Learning Disability Data Set



5.2 Characteristics of Childhood and Young Adult Cancer Survivors with A Recorded Mental Health Diagnosis on Inpatient Hospital Episode Statistics

In total, 905 (12.5%) survivors had a recorded mental health diagnosis, either as the primary reason for admission or as a listed co-morbidity in the period 1998-2015.

Characteristics of patients who had had a recorded mental health diagnosis are summarised in table 5.1b. Data on all variables (age at diagnosis, cancer type, year of diagnosis, deprivation score, ethnicity) were available for all 905 patients. Mean age at diagnosis in these patients was 19 years (interquartile range 10-25 years). Just over half were male. The most common diagnoses were germ cell tumours and lymphomas in males and non-CNS solid tumours females. The majority of patients were White British. Age at diagnosis, diagnostic group, period of diagnosis, deprivation quintile and ethnic group are also shown in figures 5.2a-5.2e, respectively. A higher proportion of individuals diagnosed with cancer in the TYA period (15-29) had a recorded mental health diagnosis on inpatient HES than those diagnosed in childhood (0-14). A higher

proportion of females had a recorded mental health diagnosis on inpatient HES than males, aside from amongst individuals with germ cell tumours, where a slightly higher proportion of males had a recorded mental health diagnosis on inpatient HES. A higher proportion of individuals with lymphomas and germ cell tumours had a recorded mental health diagnosis on inpatient HES than other tumour types. The proportion of individuals with a recorded mental health diagnosis on inpatient HES increased as deprivation fifth increased (i.e. as the population got more deprived). The proportion of White British and South Asian individuals with a recorded mental health diagnosis on inpatient HES was similar. A higher proportion of individuals diagnosed between 2000 and 2009 had a recorded mental health diagnosis on inpatient HES than those diagnosed in other time periods. Further statistical analysis to explore whether these differences are significant has been carried out and is described in section 5.6: Groups at Increased Risk of Mental Health Services Use and Co-Morbidity.

Table 5.1b Characteristics of 5 year childhood and young adult cancer survivors who had a recorded mental health diagnosis on the inpatient Hospital Episode Statistics dataset

Variable		Number with recorded mental health diagnosis (total individuals on registry)		Proportion of each group with a recorded mental health diagnosis	
		Male	Female	Male	Female
Age Group at diagnosis	0-4	58 (901)	63 (723)	6.4%	8.7%
	5-9	42 (526)	50 (390)	8.0%	12.8%
	10-14	59 (562)	52 (440)	10.5%	11.8%
	15-19	78 (519)	67 (364)	15.2%	18.4%
	20-24	108 (758)	80 (420)	14.2%	19.0%
	25-29	151 (1026)	97 (581)	14.7%	16.7%
ICCC diagnostic group	Leukaemia	68 (833)	73 (621)	8.2%	11.8%
	Lymphoma	116 (857)	97 (563)	13.5%	17.2%
	CNS	81 (692)	75 (587)	11.7%	12.8%
	Germ cell	144 (1005)	19 (138)	14.3%	13.8%

	Non-CNS solid	87 (942)	145 (1004)	9.2%	14.4%
Period of diagnosis	1974-1979	17 (230)	14 (173)	7.4%	8.1%
	1980-1984	14 (181)	18 (146)	7.7%	12.3%
	1985-1989	20 (212)	24 (174)	9.4%	13.8%
	1990-1994	64 (622)	52 (417)	10.3%	12.5%
	1995-1999	80 (718)	73 (461)	11.1%	15.8%
	2000-2004	122 (911)	101 (594)	13.4%	17.0%
	2005-2009	132 (989)	101 (652)	13.3%	15.5%
	2010-2012	47 (472)	26 (301)	10.0%	8.6%
Deprivation category (based on Townsend deprivation index)	1	73 (785)	50 (559)	9.3%	8.9%
	2	84 (824)	61 (527)	10.2%	11.6%
	3	80 (810)	72 (535)	9.9%	13.5%
	4	94 (828)	98 (529)	11.4%	18.5%
	5	165 (1088)	128 (768)	15.2%	16.7%

Ethnicity	White British	452 (3798)	370 (2566)	11.9%	14.4%
	South Asian	35 (291)	26 (198)	12.0%	13.1%
	Other	9 (159)	13 (118)	5.7%	11.0%

Figure 5.2a Age at diagnosis for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded mental health diagnosis on the Inpatient Hospital Episode Statistics Data Set

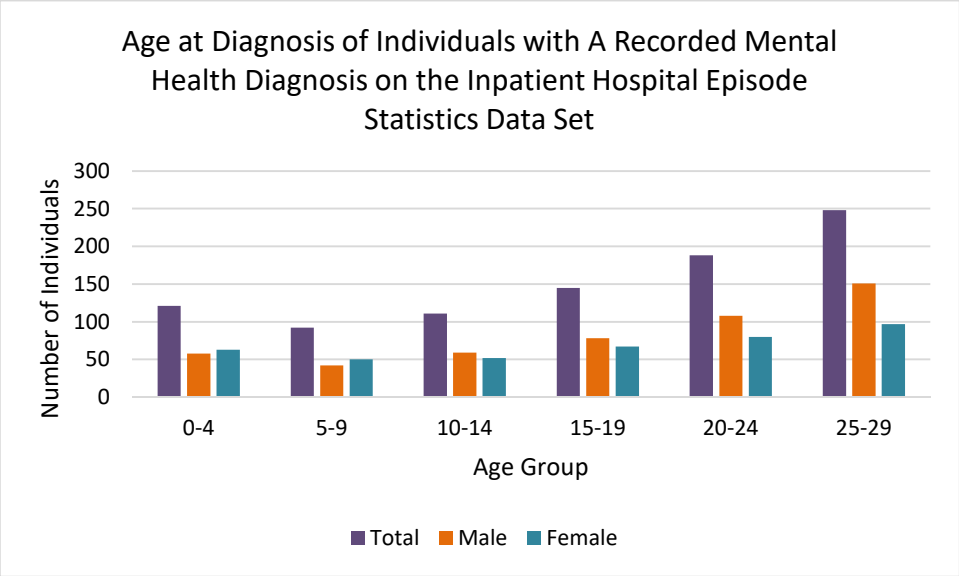


Figure 5.2b Diagnostic group for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded mental health diagnosis on the Inpatient Hospital Episode Statistics Data Set

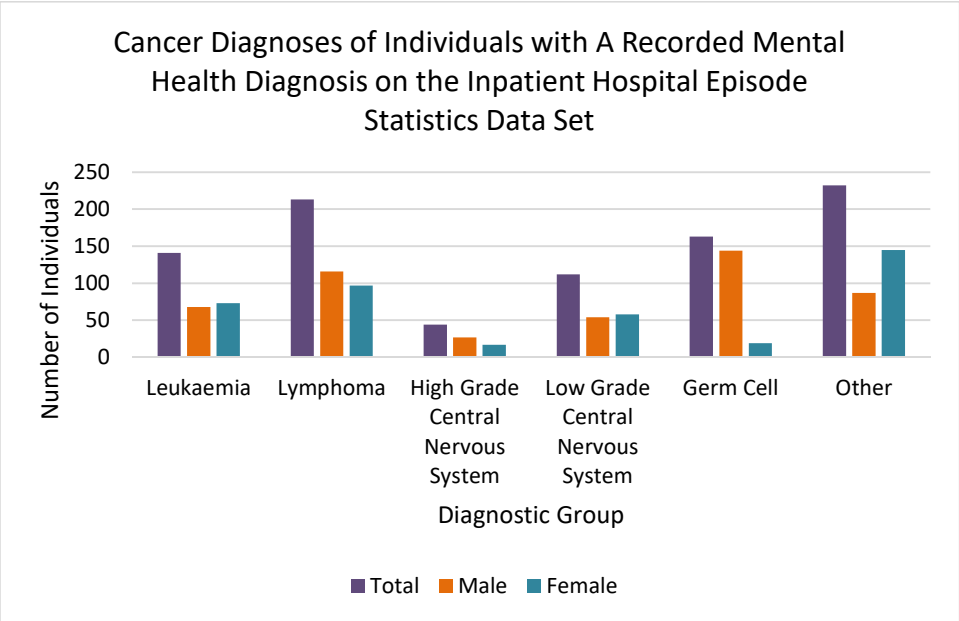


Figure 5.2c Period of diagnosis for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded mental health diagnosis on the Inpatient Hospital Episode Statistics Data Set

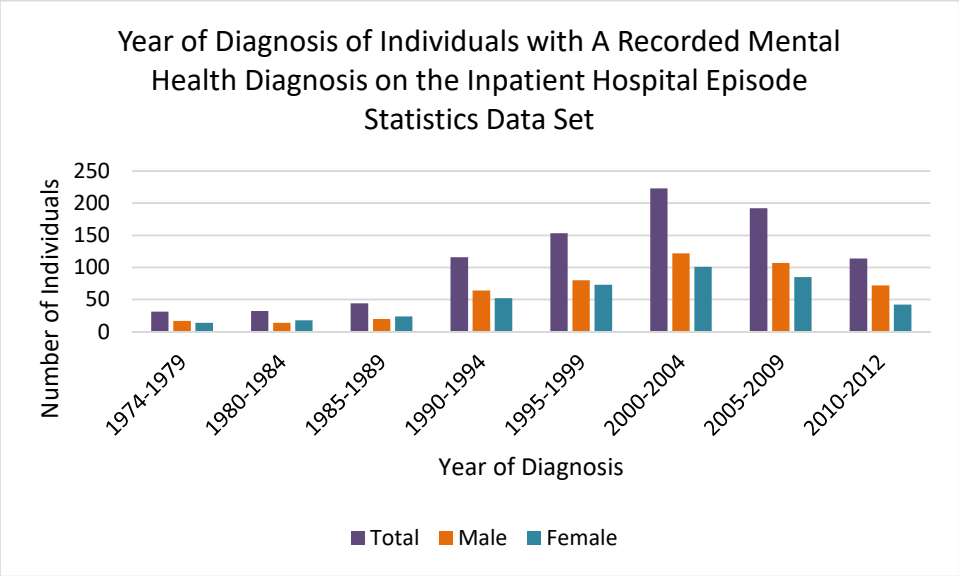


Figure 5.2d Deprivation quintile for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded mental health diagnosis on the Inpatient Hospital Episode Statistics Data Set

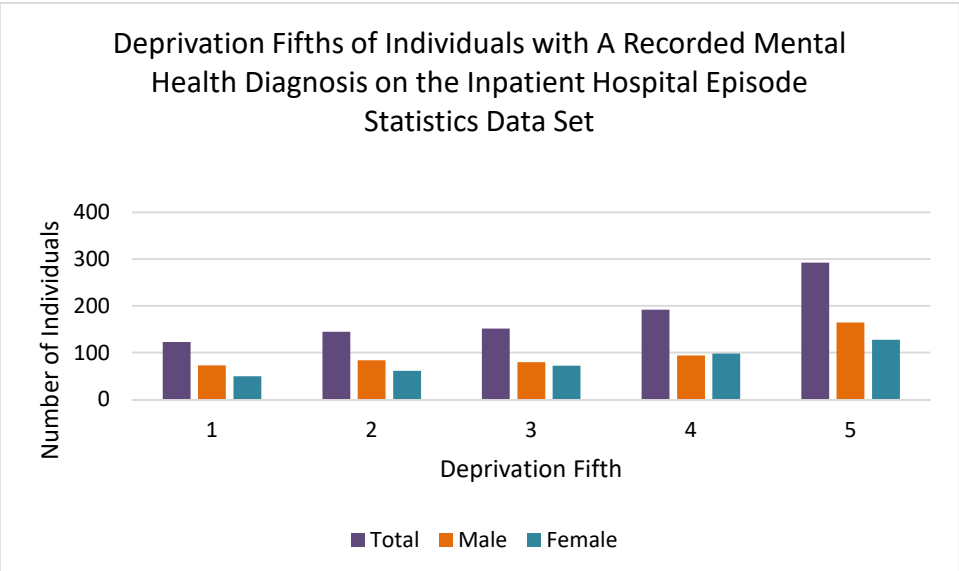
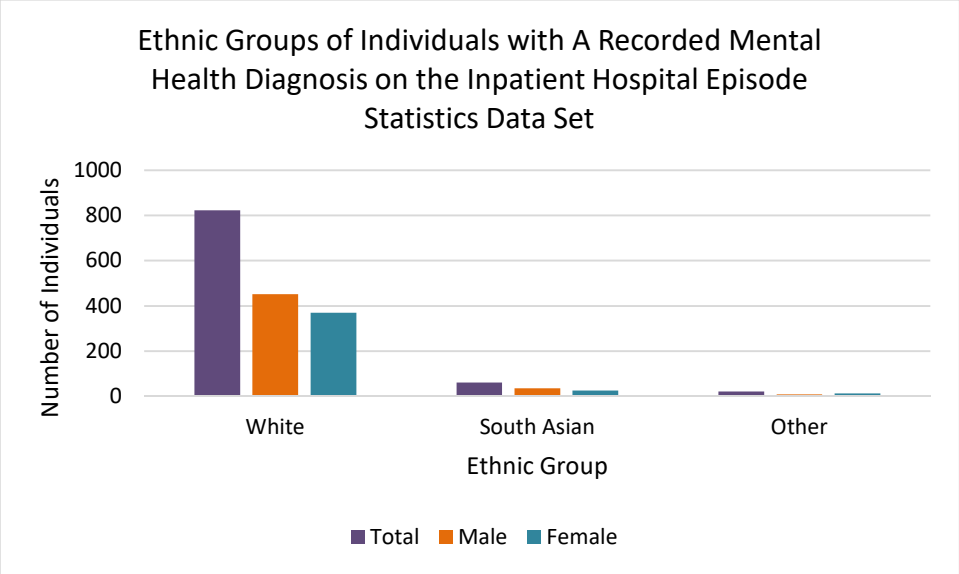


Figure 5.2e Ethnic group for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People with a recorded mental health diagnosis on the Inpatient Hospital Episode Statistics Data Set



5.3 Combined Indicators of Mental Ill Health

Some individuals with a record on the MHMDS and/or MHLDDS also had a recorded mental health diagnosis on inpatient HES.

Figure 5.3 shows the number of individuals with a recorded contact with specialist mental health services, a recorded mental health diagnosis on inpatient HES or both. Of the 777 individuals with a record of specialist mental health services use, 365 also had a recorded mental health diagnosis on inpatient HES and 412 only had an MHMDS or MHLDDS record. 540 individuals only had a recorded mental health diagnosis on inpatient HES.

In total, 1317 (18.2%) individuals had at least one indicator of mental ill health. The characteristics of these individuals are shown in table 5.1c. Ethnicity data were available for 1303 (98.9%) of these individuals. Data on sex, age at diagnosis, diagnostic group, period of diagnosis and deprivation (Townsend deprivation index) were available for all individuals. Age at diagnosis, diagnostic group, period of diagnosis, deprivation quintile and ethnic group are also shown in figures 5.4a-5.4e, respectively.

A higher proportion of individuals diagnosed in the TYA period (15-29) had at least one indicator of mental ill health than those diagnosed as children. A higher proportion of individuals with lymphomas, CNS tumours and germ cell tumours had at least one indicator of mental ill health than those with leukaemias or non-CNS solid tumours. A higher proportion of individuals diagnosed with cancer in 2005-2009 had at least one indicator of mental ill health than those diagnosed in other periods. A higher proportion of individuals from more deprived fifths (4 and 5) had at least one indicator of mental ill health that those from less deprived fifths. A higher proportion of White British individuals had at least one indicator of mental ill health than other ethnic groups. Section 5.6: Groups at Increased Risk of Mental Health Services Use and Co-Morbidity uses logistic regression to determine which of these differences are statistically significant.

Figure 5.3 Venn diagram showing the numbers of individuals with a recorded mental health contact on Mental Health Services Data Set or Mental Health and Learning Disabilities Data Set, a recorded mental health diagnosis on the inpatient Hospital Episode Statistics dataset, and where these overlapped.

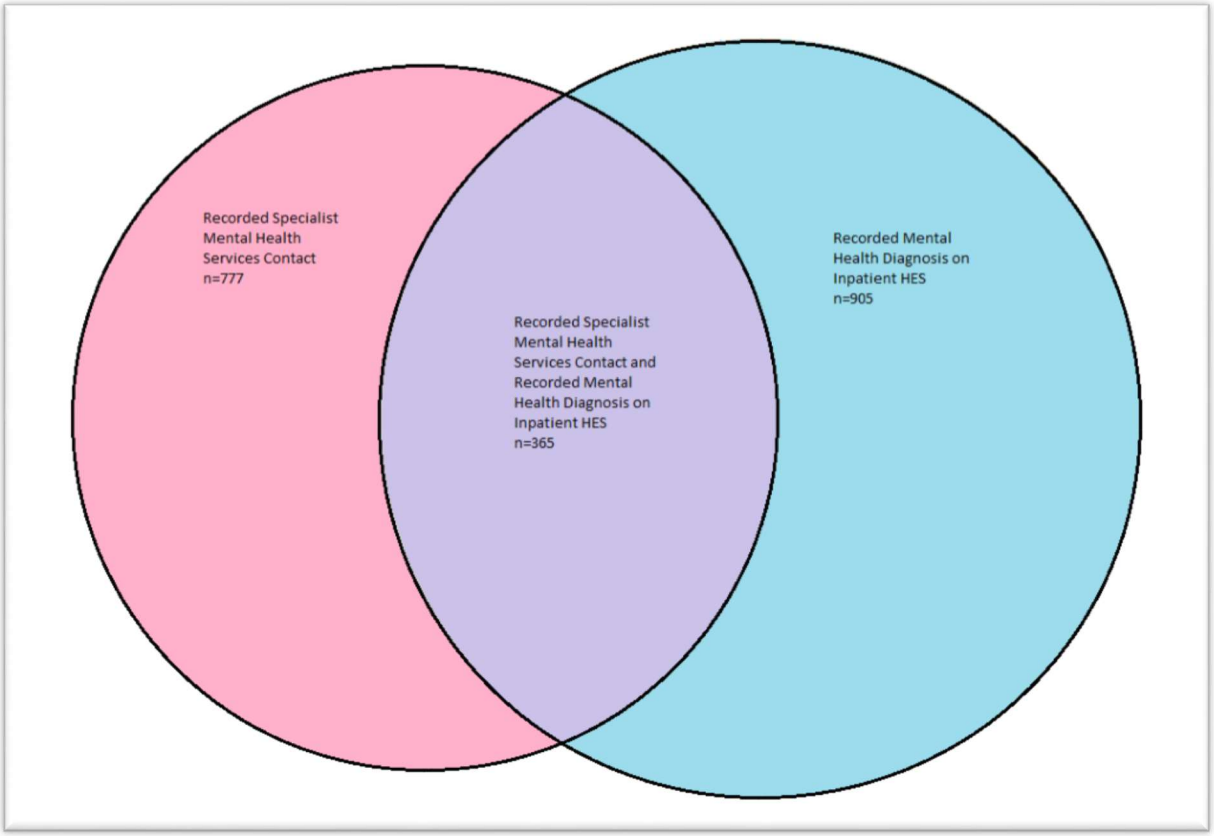


Table 5.1c Characteristics of 5 year childhood and young adult cancer survivors who had either a recorded mental health contact on the Mental Health Services Data Set or the Mental Health and Learning Disabilities Data Set, a recorded mental health diagnosis on the inpatient hospital episode statistics dataset, or both.

Variable		Number with recorded mental health contact, diagnosis or both (total individuals on registry)		Proportion of each group with recorded mental health contact, diagnosis or both	
		Male	Female	Male	Female
Age Group at diagnosis	0-4	91 (901)	96 (723)	10.1%	13.3%
	5-9	76 (526)	60 (390)	14.4%	15.4%
	10-14	93 (562)	75 (440)	16.5%	17.0%
	15-19	112 (519)	96 (364)	21.6%	26.4%
	20-24	159 (758)	110 (420)	21.0%	26.2%
	25-29	209 (1026)	140 (581)	20.4%	24.1%
ICCC diagnostic group	Leukaemia	110 (833)	99 (621)	13.2%	15.9%
	Lymphoma	167 (857)	131 (563)	19.5%	23.3%
	CNS	126 (692)	120 (587)	18.6%	20.4%
	Germ cell	204 (1005)	26 (138)	20.3%	18.8%

	Non-CNS solid	133 (942)	201 (1004)	14.1%	20.0%
Period of diagnosis	1974-1979	27 (230)	20 (173)	11.7%	11.6%
	1980-1984	22 (181)	25 (146)	12.2%	17.1%
	1985-1989	30 (212)	43 (174)	14.2%	24.7%
	1990-1994	102 (622)	80 (417)	16.4%	19.2%
	1995-1999	124 (718)	97 (461)	17.3%	21.0%
	2000-2004	169 (911)	129 (594)	18.6%	21.7%
	2005-2009	202 (989)	145 (652)	20.4%	22.2%
	2010-2012	64 (472)	38 (301)	13.6%	12.6%
Deprivation category (based on Townsend deprivation index)	1	112 (785)	82 (559)	14.3%	14.7%
	2	130 (824)	98 (527)	15.8%	18.6%
	3	125 (810)	98 (535)	15.4%	18.3%
	4	139 (828)	129 (529)	16.8%	24.4%
	5	234 (1088)	170 (768)	21.5%	22.1%

Ethnicity	White British	667 (3798)	518 (2566)	17.6%	20.2%
	South Asian	50 (291)	36 (198)	17.2%	18.2%
	Other	14 (159)	18 (118)	8.8%	15.3%

Figure 5.4a Age at diagnosis for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People, and those with at least one indicator of mental ill health

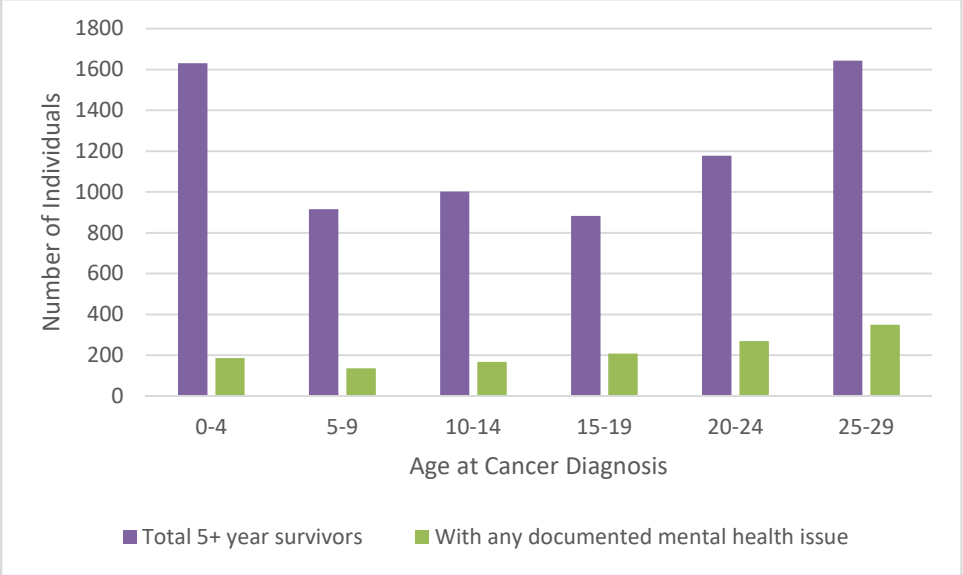


Figure 5.4b Diagnostic group for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People, and those with at least one indicator of mental ill health

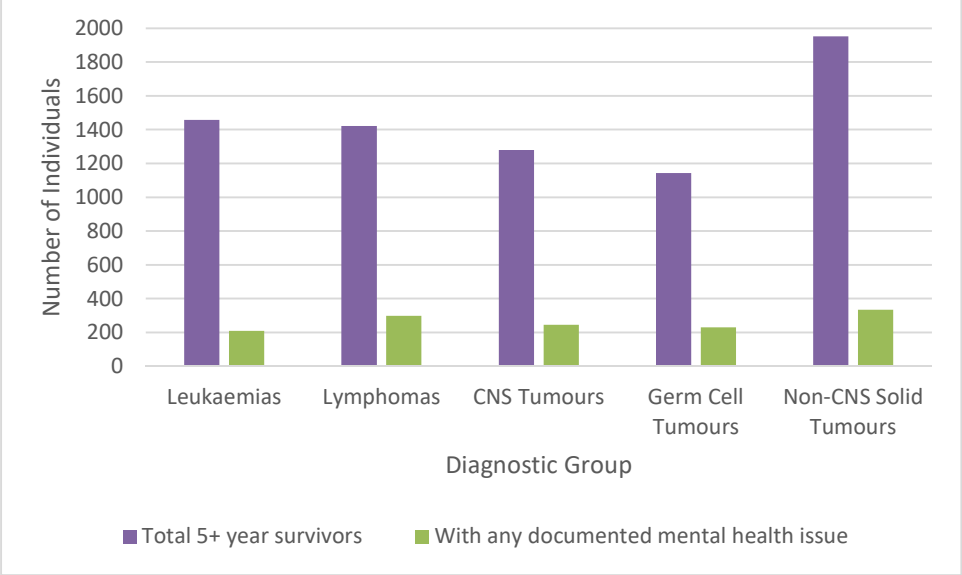


Figure 5.4c Period of diagnosis for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People, and those with at least one indicator of mental ill health

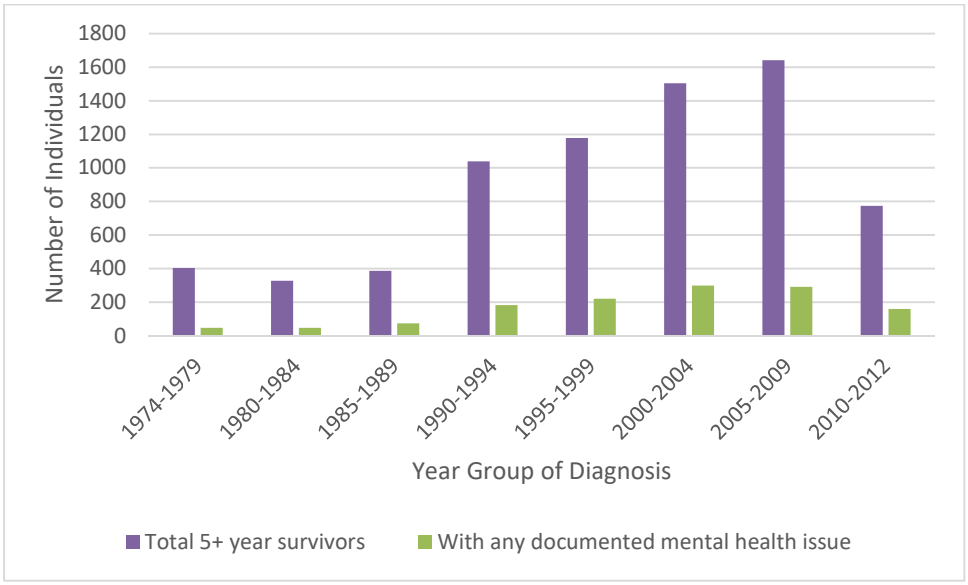


Figure 5.4d Deprivation quintile for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People, and those with at least one indicator of mental ill health

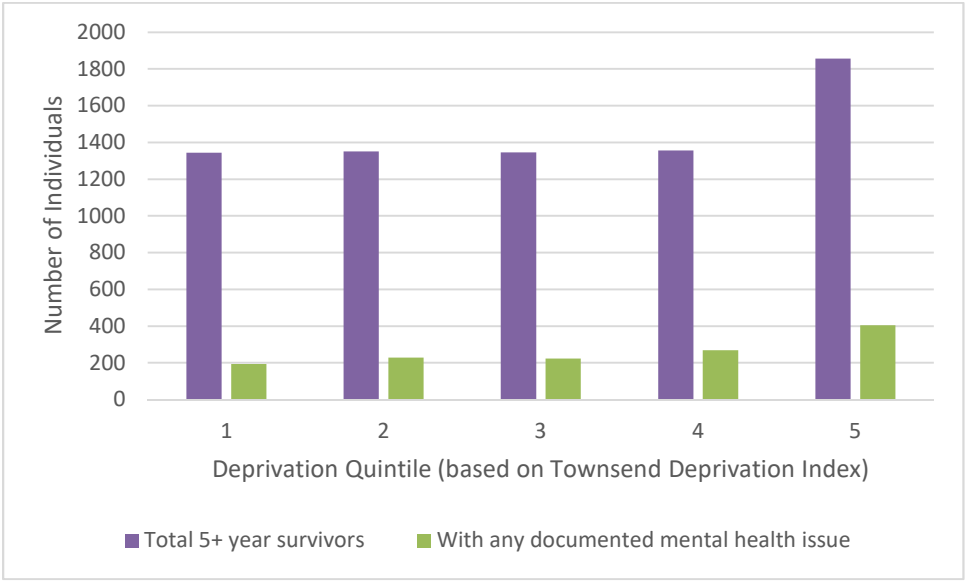
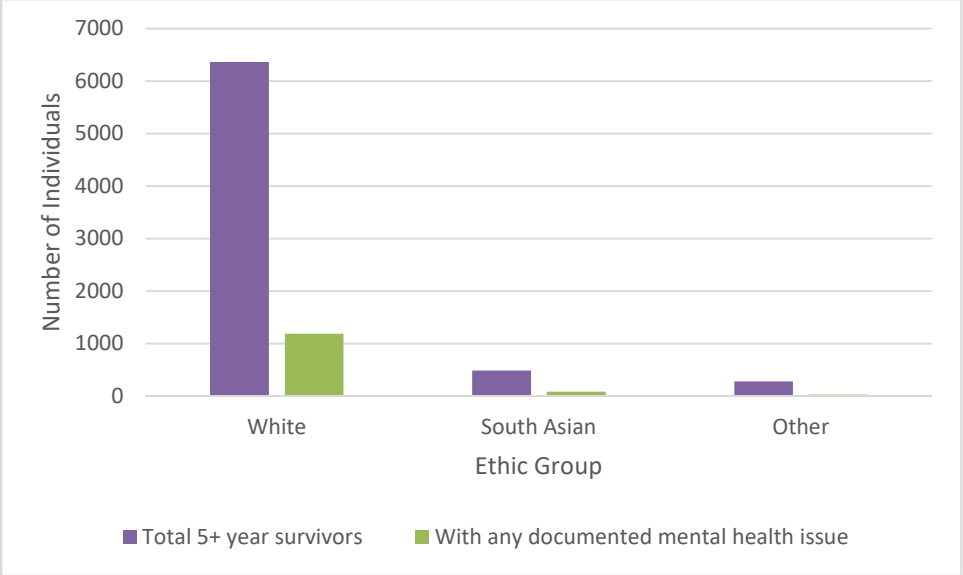


Figure 5.4e Ethnic group for all 5+ year survivors on the Yorkshire Specialist Register of Cancer in Children and Young People, and those with at least one indicator of mental ill health



5.4 Comparison between Mental Health Services Use amongst Individuals on the Yorkshire Specialist Register of Cancer in Children and Young People and the Yorkshire Population as a Whole

HES data on mental health contacts were available for each financial year from 2006-07 to 2015-16, although the data for 2015-16 were only available for half of the financial year; this was because of the way data were recorded changed half way through this year, as described in the Methods chapter. Individual-level data were obtained for all individuals on the YSRCCYP. Aggregated data, giving the number of individuals who had an MHMDS or MHLDDS record (i.e. the number of individuals who had accessed specialist mental health care services) in each year, were also obtained for the population of Yorkshire.

Tables showing full details of the population of Yorkshire, the number of individuals with a mental health care service contact, the cohort characteristics on the YSRCCYP (the total number of individuals on the YSRCCYP who were still alive that year) and the number of individuals on the YSRCCYP with a

mental health care service contact for each financial year are provided in Appendix D: Mental Health Contacts Per Financial Year 2006-07 to 2015-16.

In the financial year 2006-07, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 5 to 9, male 10 to 14, male 15 to 19, female 10 to 14, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39, female 40 to 44 and female 45 to 49. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49 and female 5 to 9.

In the financial year 2007-08, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, female 10 to 14, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 40 to 44, male 45 to 49, female 5 to 9 and female 45 to 49.

In the financial year 2008-09, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, male 30 to 34, male 40 to 44, female 5 to 9, female 10 to 14, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34 and female 40 to 44. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 25 to 29, male 35 to 39, male 45 to 49, female 35 to 39 and female 45 to 49.

In the financial year 2009-10, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, female 5 to 9, female 10 to 14, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34 and female 45 to 49. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 25 to 29, male 30 to 34, male 35 to

39, male 40 to 44, male 45 to 49, male 50 to 54, female 35 to 39 female 40 to 44 and female 50 to 54.

In the financial year 2010-11, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, male 40 to 44, male 45 to 49, female 5 to 9, female 10 to 14, female 20 to 24, female 25 to 29, female 30 to 34 and female 45 to 49. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 25 to 29, male 30 to 34, male 35 to 39, male 50 to 54, female 15 to 19, female 35 to 39 female 40 to 44 and female 50 to 54.

In the financial year 2011-12, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 10 to 14, male 15 to 19, male 45 to 49, male 50 to 54, female 5 to 9, female 15 to 19, female 20 to 24, female 25 to 29, and female 50 to 54. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 5 to 9, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 10 to 14, female 30 to 34, female 35 to 39, female 40 to 44 and female 45 to 49.

In the financial year 2012-13, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 10 to 14, male 15 to 19, male 20 to 24, male 50 to 54, female 5 to 9, female 20 to 24, female 25 to 29, and female 50 to 54. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 5 to 9, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49, female 10 to 14, female 15 to 19, female 30 to 34, female 35 to 39, female 40 to 44 and female 45 to 49.

In the financial year 2013-14, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS in the groups male 10 to 14, male 15 to 19, male 20 to 24, male 45 to 49, female 20 to 24 and female 25 to 29. There were higher proportions of

individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS in the groups male 5 to 9, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 50 to 54, female 5 to 9, female 10 to 14, female 15 to 19, female 30 to 34, female 35 to 39, female 40 to 44, female 45 to 49 and female 50 to 54.

In the financial year 2014-15, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHMDS or MHLDDS in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, male 25 to 29, female 25 to 29 and female 50 to 54. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHMDS or MHLDDS in the groups male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49, male 50 to 54, male 55 to 59, female 5 to 9, female 10 to 14, female 15 to 19, female 20 to 24, female 30 to 34, female 35 to 39, female 40 to 44, female 45 to 49 and female 55 to 59.

In the partial financial year 2015-16, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a record on the MHLDDS in the groups male 10 to 14, male 45 to 49 and female 10 to 14. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a records on the MHLDDS in the groups male 5 to 9, male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 50 to 54, male 55 to 59, female 5 to 9, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39, female 40 to 44, female 45 to 49, female 50 to 54 and female 55 to 59.

In order to compare the rates of specialist mental health service access between the Yorkshire population and the YSRCCYP, standardised incidence ratios were calculated. These are shown in Table 5.2, and presented as a forest plot in figure 5.5. In order to make valid calculations, and to avoid under-estimating the use of mental health services in the Yorkshire population, all small number suppressed values were assumed to be 4. This was because the calculation couldn’t be performed without a number being inserted, and the maximum possible number of contacts which could be reported as suppressed was 4. It would have been possible to assume that these suppressed values were 1, 2 or 3 instead, but by choosing 4, this ensures that the Yorkshire

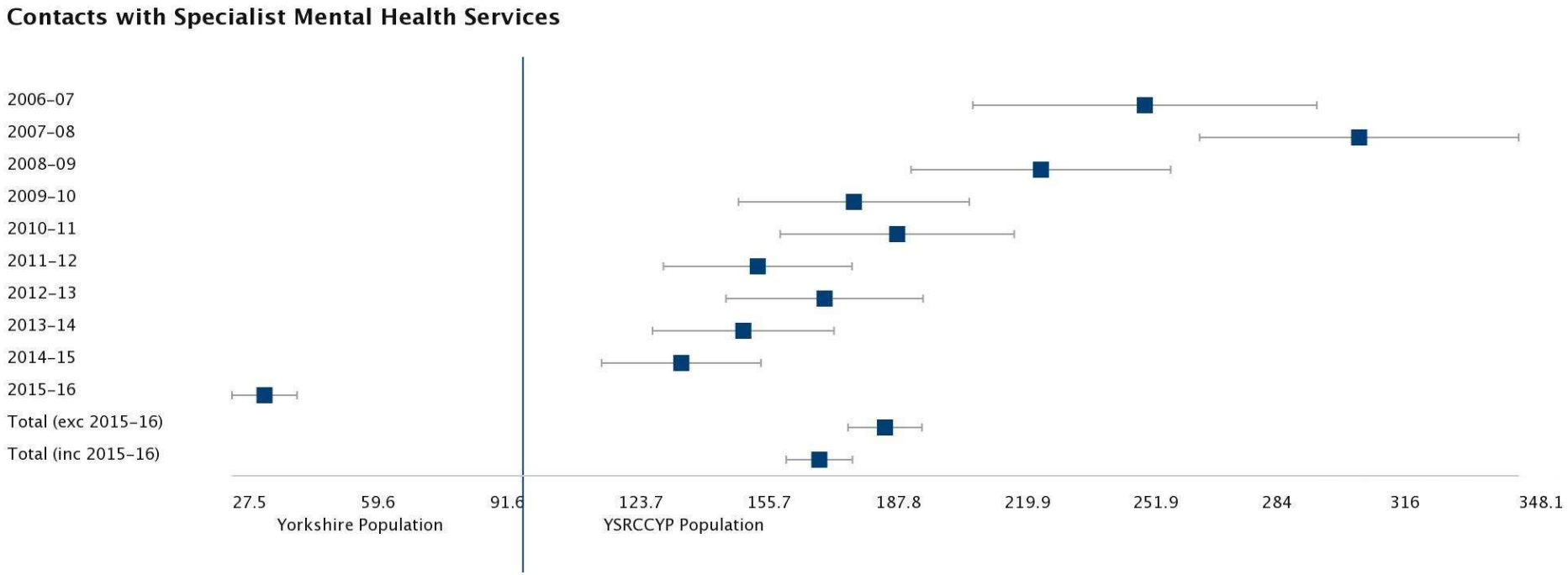
population contacts are not being over estimated. This was the case on 3 occasions, for females aged 5-9 in 2008-09, 2009-10 and 2011-12.

Table 5.2 Standardised incidence ratios for mental health services use in the Yorkshire Specialist Register of Cancer in Children and Young People population compared to the Yorkshire population[f].

Year	Observed Contacts	Expected Contacts	Standardised Incidence Ratio	95% Confidence Intervals	
2006-07	139	55.1	252.2	212.1	297.8
2007-08	236	77.0	306.4	268.6	348.1
2008-09	197	86.7	227.3	196.7	261.4
2009-10	158	87.4	180.7	153.7	211.2
2010-11	173	90.3	191.6	164.1	222.4
2011-12	179	113.9	157.2	135.0	182.0
2012-13	200	115.0	173.9	150.6	199.7
2013-14	185	120.4	153.7	132.3	177.5
2014-15	194	140.2	138.4	119.6	159.3
2015-16	76	217.8	34.9	27.5	43.7
Total (excluding 2015-16)	1,661	874.1	190.0	181.0	199.4
Total (including 2015-16)	**1,737**	**1000.0**	**173.7**	**165.6**	**182.1**

[f] Expected contacts were calculated by taking the number of contacts seen in the Yorkshire population and multiplying these by the population on the YSRCCYP

Figure 5.4 Forest plot showing standardised incidence ratios for mental health services use in the Yorkshire Specialist Register of Cancer in Children and Young People population compared to the Yorkshire population.[g].



[g] Plot made using DistillerSR Forest Plot Generator from Evidence Partners[399]

There was a significantly greater rate of mental health services use amongst the YSRCCYP population than the Yorkshire population for all years except 2015-16, which was initially left out of the calculation as data from this year was incomplete. When the all years are considered together, there remained a significantly greater rate of mental health services use in the YSRCCYP population. Adding in the 2015-16 data only marginally impacted on the overall values seen.

Reasons for this increased rate of mental health services use amongst the YSRCCYP population are considered in section 7.4.1 Discussion, Strengths and Limitations of the Mental Health Work. As stated in the methods section, the way data were recorded on the data sets changed part way through the financial year 2015-16, and data were only available for part of the year. Inaccurate recording as a result may explain the anomalous findings for this year compared to other time periods.

5.5 Comparison between Mental Health Co-Morbidity amongst Individuals on the Yorkshire Specialist Register of Cancer in Children and Young People and the Yorkshire Population

Inpatient HES data were available for each financial year from 1997-98 to 2016-27. Individual-level data were obtained for all individuals on the YSRCCYP and for the population of Yorkshire. Mental health diagnoses were identified from the “diagnosis” field within inpatient HES (see Chapter 3: Data Sources and Methods, Section 3.3.2 Hospital Admitted Patient Care Activity Dataset for list of ICD-10 codes classed as “mental health diagnoses” for the purposes of this work). Data were available for individuals under 45 years old from 1997-98 to 2008-09, for individuals up to 49 years old from 2009-10 to 2010-11 and for individuals up to 59 years old from 2011-12 to 2016-17.

Tables showing the population of Yorkshire, the number of individuals with a documented mental health diagnosis on inpatient HES, the population on the YSRCCYP (the total number of individuals on the YSRCCYP who were still alive that year) and the number of individuals on the YSRCCYP with a mental health diagnosis on inpatient HES for each financial year are provided in

Appendix E: Mental Health Co-Morbidity Per Financial Year 1997-98 to 2016-17.

In the financial year 1997-98, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 10 to 14, male 30 to 34, and female 20 to 24. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 15 to 19, male 20 to 24, male 25 to 29, male 35 to 39, male 40 to 44, female 5 to 9, female 10 to 14, female 15 to 19, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 1998-99, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 30 to 34 and male 35 to 39. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, male 25 to 29, male 40 to 44, female 5 to 9, female 10 to 14, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 1999-2000, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the group male 10 to 14 only. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to 9, female 10 to 14, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 2000-01, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 35 to 39 and female 15 to 19 only. There were higher proportions of individuals from the Yorkshire

population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 40 to 44, female 5 to 9, female 10 to 14, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 2001-02, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 10 to 14, male 20 to 24, female 15 to 19 and female 20 to 24. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 15 to 19, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to 9, female 10 to 14, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 2002-03, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 10 to 14, male 40 to 44 and female 15 to 19. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, female 5 to 9, female 10 to 14, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 2003-04, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, female 10 to 14, female 20 to 24 and female 40 to 44. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to 9, female 15 to 19, female 25 to 29, female 30 to 34 and female 35 to 39.

In the financial year 2004-05, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 10 to 14 and female 15 to 19 only. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to 9, female 10 to 14, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 2005-06, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, female 10 to 14, female 15 to 19 and female 25 to 29. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to 9, female 20 to 24, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 2006-07, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 10 to 14, male 15 to 19, female 15 to 19, female 30 to 34 and female 40 to 44. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to 9, female 10 to 14, female 20 to 24, female 25 to 29 and female 35 to 39.

In the financial year 2007-08, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups female 15 to 19 and female 30 to 34 only. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to

9, female 10 to 14, female 20 to 24, female 25 to 29, female 35 to 39 and female 40 to 44.

In the financial year 2008-09, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, male 15 to 19, female 5 to 9, female 15 to 19 and female 20 to 24. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 10 to 14, female 25 to 29, female 30 to 34, female 35 to 39 and female 40 to 44.

In the financial year 2009-10, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 45 to 49, female 10 to 14, female 15 to 19, female 25 to 29 and female 30 to 34. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, female 5 to 9, female 20 to 24, female 35 to 39, female 40 to 44 and female 45 to 49.

In the financial year 2010-11, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, female 10 to 14 and female 20 to 24. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49, female 5 to 9, female 15 to 19, female 25 to 29, female 30 to 34, female 35 to 39, female 40 to 44 and female 45 to 49.

In the financial year 2011-12, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9 and male 10 to 14 only. There were higher proportions of individuals from the Yorkshire population

than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49, male 50 to 54 female 5 to 9, female 10 to 14, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39, female 40 to 44, female 45 to 49 and female 50 to 54.

In the financial year 2012-13, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, male 15 to 19, male 20 to 24, female 5 to 9 and female 15 to 19. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49, male 50 to 54, female 10 to 14, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39, female 40 to 44, female 45 to 49 and female 50 to 54.

In the financial year 2013-14, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 15 to 19, female 5 to 9 and female 10 to 14. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 10 to 14, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49, male 50 to 54, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39, female 40 to 44, female 45 to 49, female 50 to 54 and female 55 to 59.

In the financial year 2014-15, there were higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient HES in the groups male 5 to 9, male 10 to 14, and female 10 to 14. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES in the groups male 15 to 19, male 20 to 24, male 25 to 29, male 30 to 34, male 35 to 39, male 40 to 44, male 45 to 49, male 50 to 54, male 55 to 59, female 5 to 9, female 15 to 19, female 20 to 24, female 25 to 29, female 30 to 34, female 35 to 39, female 40 to 44, female 45 to 49, female 50 to 54 and female 55 to 59.

In the financial year 2015-16, there were no groups with higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES all groups.

In the partial financial year 2016-17, there were no groups with higher proportions of individuals from the YSRCCYP than from the Yorkshire population with a recorded mental health diagnosis on inpatient. There were higher proportions of individuals from the Yorkshire population than from the YSRCCYP with a recorded mental health diagnosis on inpatient HES all groups.

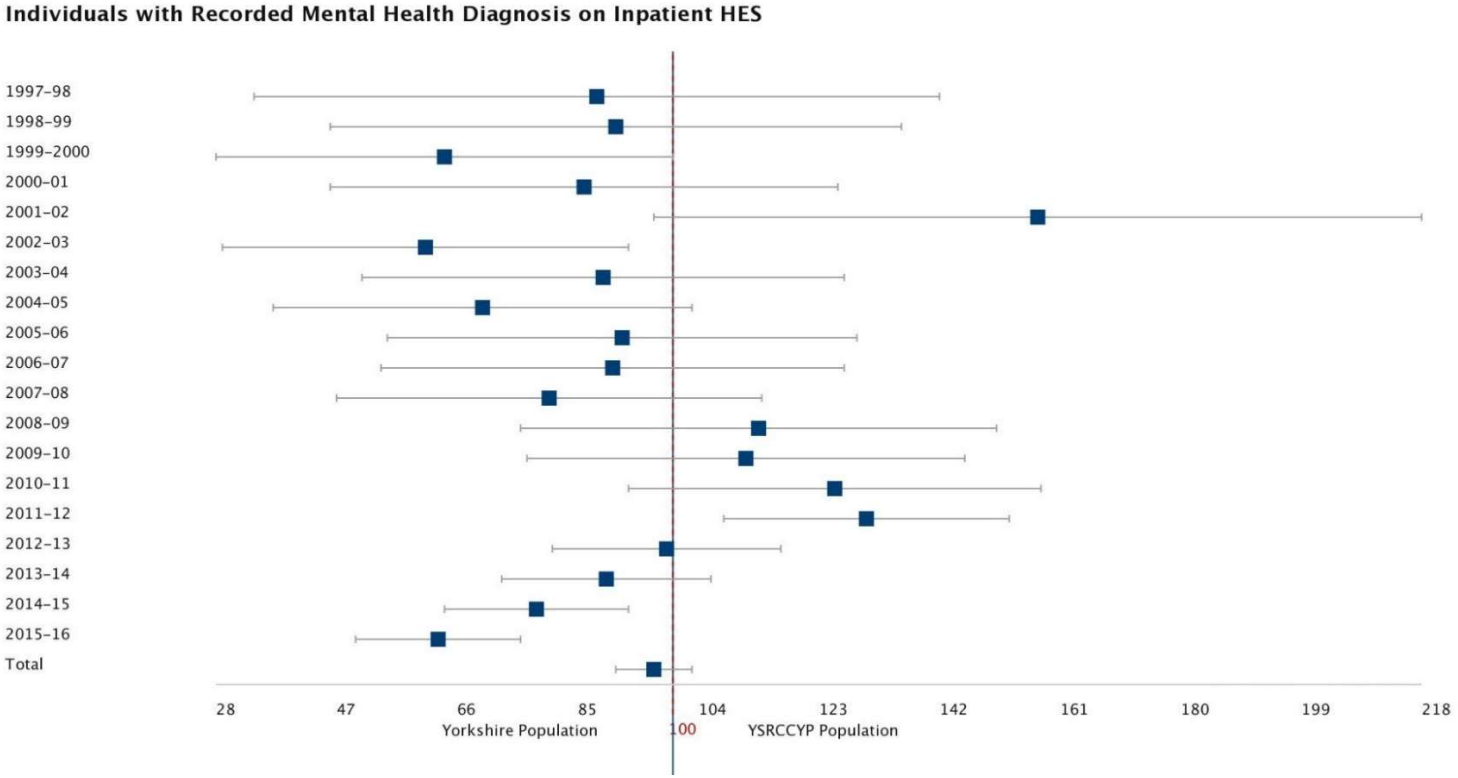
In order to compare the rates of mental health diagnoses (as recorded on inpatient HES) between the Yorkshire population and the YSRCCYP, standardised incidence ratios were calculated. These are shown in Table 5.3, and presented as a forest plot in figure 5.6.

Table 5.3 Standardised incidence ratios for mental health diagnoses Yorkshire Specialist Register of Cancer in Children and Young People population compared to the Yorkshire population. Expected contacts were calculated by taking the number of contacts seen in the Yorkshire population and multiplying these by the population on the Yorkshire Specialist Register of Cancer in Children and Young People.

Year	Observed Contacts	Expected Contacts	Standardised Incidence Ratio	95% Confidence Intervals	
1997-98	9	12	75	34	142
1998-99	15	18	83	46	136
1999-2000	11	20	56	28	100
2000-01	17	22	79	46	126
2001-02	26	17	149	97	218
2002-03	13	24	54	29	93
2003-04	21	25	83	51	127
2004-05	17	26	64	37	103
2005-06	24	28	86	55	129
2006-07	24	28	85	54	127
2007-08	22	29	75	47	114
2008-09	35	32	109	76	151
2009-10	40	37	107	77	146
2010-11	58	48	122	93	158
2011-12	133	103	129	108	153
2012-13	119	122	98	81	117
2013-14	119	135	88	73	106
2014-15	111	144	77	64	93

2015-16	92	148	62	50	76
Total	**1029**	**1059**	**97**	**91**	**103**

Figure 5.5 Forest plot showing standardised incidence ratios for mental health diagnoses on inpatient Hospital Episode Statistics in the Yorkshire Specialist Register of Cancer in Children and Young People population compared to the Yorkshire population.[h]



[h] Plot made using DistillerSR Forest Plot Generator from Evidence Partners[399].

There was no significant difference between rates of mental health diagnoses on inpatient HES between the Yorkshire population and the YSRCCYP. For the years 2002-03, 2014-15 and 2015-16 there was a significantly lower rate of mental health diagnoses amongst individuals on the YSRCCYP compared to the Yorkshire population, and for the year 2011-12, there was a significantly higher rate of mental health diagnoses amongst individuals on the YSRCCYP compared to the Yorkshire population. When data on all years were combined, there was no significant difference in rates of mental health diagnoses in individuals on the YSRCCYP compared to the Yorkshire population.

Reasons for the lack of difference between rates of recorded mental health diagnoses on inpatient HES are discussed in section 7.4.1 Discussion, Strengths and Limitations of the Mental Health Work

5.6 Groups at Increased Risk of Mental Health Services Use and Co-Morbidity

The results demonstrate an increased rate of mental health services use amongst individuals on the YSRCCYP compared to the wider Yorkshire population. There did not appear to be increased mental health co-morbidity documented on inpatient HES amongst individuals on the YSRCCYP compared to the wider Yorkshire population. Logistic regression was used to determine whether there were certain groups within the YSRCCYP who were at particular increased risk of mental health services use, mental health co-morbidity recorded on inpatient HES or both. The adjustments made are based on casual inference models and the DAGs described in Chapter 3: Data Sources and Methods.

5.6.1 Hypotheses

It was hypothesised that:

- Individuals diagnosed aged 13-24 would be at increased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES.

- Individuals from a more deprived background would be at increased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES.
- Individuals from a South Asian background would be at decreased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES.
- Females would be at increased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES.
- Individuals with more advanced, higher stage disease, or higher grade CNS tumours, would be at increased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES.
- Individuals treated at a specialist TYA unit would be at decreased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES.
- Individuals treated with radiotherapy, or combined chemo- and radiotherapy, would be at decreased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES, compared to those treated with chemotherapy alone or neither chemo- nor radiotherapy.
- Individuals with NCSI level 3 would be at increased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES compared to individuals with NCSI level 1 or 2.
- Individuals with CNS tumours would be at increased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES compared to individuals with other tumour types.
- Individuals diagnosed longer ago would be at increased risk of inclusion on the MHMDS/MHLDDS or having a recorded mental health diagnosis on inpatient HES.

5.6.2 Age at diagnosis

Age at diagnosis was explored as a potential risk factor. As discussed in the introduction, those diagnosed at 13-24 years old are a particular group of interest, and thus this group was compared to those older and younger at diagnosis. The risk of mental health services use and mental health diagnosis was compared between individuals aged 13-24 and those older or younger at the time of diagnosis. Table 5.6a shows the number of individuals in each age group, as well as the odds ratio of mental health services use for those aged 13-24 and 25-29 at diagnosis, compared to those aged 12 and under. The odds ratio of mental health services use for those aged 25-29 compared to those aged 13-24 at diagnosis is also shown. Table 5.6b shows the odds ratio of having a recorded mental health diagnosis on inpatient HES. Table 5.6c shows the odds ratio of having either a recorded mental health services contact, a recorded mental health diagnosis or both.

Table 5.6a Odds ratios of mental health services use for individuals diagnosed with cancer at different ages[i]

Age Group	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
0-12	3073	229	Reference		
13-24	2537	338	1.93	1.61	2.30
25-29	1643	210	1.83	1.50	2.23

[i] adjusted for deprivation (Townsend deprivation index) and sex

Table 5.6b Odds ratios of mental health diagnoses on inpatient Hospital Episode Statistics for individuals diagnosed with cancer at different ages[j]

Age Group	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
0-12	3073	273	Reference		
13-24	2537	384	1.86	1.57	2.19
25-29	1643	248	1.84	1.53	2.22

Table 5.6c Odds ratios of mental health services use, mental health diagnoses on inpatient Hospital Episode Statistics, or both for individuals diagnosed with cancer at different ages[k]

Age Group	Number of Individuals	Number with Record of Mental Ill Health	Odds ratio of Record of Mental Ill Health	95% Confidence Intervals	
0-12	3073	403	Reference		
13-24	2537	565	1.92	1.67	2.21
25-29	1643	349	1.80	1.54	2.11

Individuals aged 13-24 and 25-29 at diagnosis were significantly more likely than individuals aged 12 and under at diagnosis to have a recorded mental health services contact or mental health diagnosis on inpatient HES. There was no significant difference in likelihood of mental health services contact between those aged 13-24 and those aged 25-29 at diagnosis.

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[j] adjusted for deprivation (Townsend deprivation index) and sex

[k] adjusted for deprivation (Townsend deprivation index) and sex

5.6.3 Deprivation

It was hypothesised that being from a more deprived background would be associated with increased mental health services use, due to the social and financial difficulties these individuals face leading to a suspected increased incidence of mental health difficulties. Logistic regression was performed using both raw Townsend deprivation index and deprivation fifths, as using the raw index scores gives more detailed information, but breaking the cohort into fifths allowed exploration of a trend which may not be linear. The odds ratio of mental health services use is shown in table 6.7a, whilst odds ratio of mental health diagnosis on inpatient HES is shown in table 6.7b. Table 6.7c shows the odds ratio of having either a recorded mental health services contact, a recorded mental health diagnosis or both.

Table 5.7a Odds ratios of mental health services use for individuals in each deprivation quintile and for individuals from areas with increasingly Townsend deprivation index[l]

Deprivation category (based on Townsend deprivation index)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
5 (most deprived)	1856	241	Reference		
4	1357	149	0.78	0.63	0.98
3	1345	135	0.68	0.54	0.86
2	1351	137	0.70	0.55	0.88
1 (least deprived)	1344	115	0.57	0.45	0.73
Townsend deprivation index (continuous - per 1 point increase in deprivation)	n/a		1.06	1.03	1.08

[l] adjusted for ethnicity and sex

Table 5.7b Odds ratios of mental health diagnoses on inpatient Hospital Episode Statistics for individuals in each deprivation quintile and for individuals from areas with increasingly Townsend deprivation index[m]

Deprivation category (based on Townsend deprivation index)	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
5 (most deprived)	1856	293	Reference		
4	1357	198	0.88	0.72	1.07
3	1345	152	0.67	0.55	0.83
2	1351	145	0.63	0.51	0.79
1 (least deprived)	1344	123	0.53	0.42	0.66
Townsend deprivation index (per 1 point increase in deprivation)	n/a		1.06	1.04	1.08

[m] adjusted for ethnicity and sex

Table 5.7c Odds ratios of mental health diagnoses on inpatient Hospital Episode Statistics, recorded mental health contacts or both for individuals in each deprivation quintile and for individuals from areas with increasingly Townsend deprivation index[n]

Deprivation category (based on Townsend deprivation index)	Number of Individuals	Number with Record of Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
5 (most deprived)	1856	404	Reference		
4	1357	268	0.89	0.75	1.05
3	1345	223	0.71	0.59	0.85
2	1351	228	0.72	0.61	0.87
1 (least deprived)	1344	194	0.60	0.50	0.73
Townsend deprivation index (per 1 point increase in deprivation)	n/a		1.05	1.03	1.07

Individuals from less deprived areas were significantly less likely than those in the most deprived group to have had recorded mental health services use or recorded mental health diagnosis on inpatient HES. There was a small but significant increase in risk of mental health services use and risk of mental health diagnosis for each one point increase in Townsend deprivation

[n] adjusted for ethnicity and sex

index. Similar results were seen when both indicators of mental ill health were combined.

5.6.4 Ethnicity

Ethnicity was also explored as a potential factor which would affect likelihood of mental health services use. It was hypothesised that individuals from a South Asian background would be less likely to have mental health services contacts than White British individuals, due to cultural stigma surrounding mental illness[356,357]. The odds ratios of mental health services use are shown in table 5.8a, risks of mental health diagnosis on inpatient HES are shown in table 5.8b and risks of either mental health services use, mental health diagnosis or both are shown in table 5.8c.

Table 5.8a Odds ratios of mental health services use for individuals in different ethnic groups[o]

Ethnic Group	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
White British	6364	693	Reference		
South Asian	489	47	0.87	0.64	1.19
Other	277	23	0.74	0.48	1.14

[o] no additional model adjustment required

Table 5.8b Odds ratios of mental health diagnoses on inpatient Hospital Episode Statistics for individuals in different ethnic groups [p]

Ethnic Group	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
White British	6364	822	Reference		
South Asian	489	61	0.96	0.73	1.27
Other	277	22	0.58	0.37	0.90

Table 5.8c Odds ratios of mental health services use and/or mental health diagnoses on inpatient Hospital Episode Statistics for individuals in different ethnic groups [q]

Ethnic Group	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
White British	6364	1185	Reference		
South Asian	489	86	0.93	0.73	1.19
Other	277	32	0.57	0.39	0.83

[p] no additional model adjustment required

[q] no additional model adjustment required

There was no statistically significant difference between risks of mental health services use between different ethnic groups, although a slightly lower risk of mental health services use was seen in South Asian and other ethnicities compared to White British. A significant reduction in likelihood of mental health diagnosis on inpatient HES was seen in the “other” ethnic group compared to White British individuals. When both indicators of mental ill health were combined, the “other” group had significantly reduced risk of mental ill health compared to the White British group.

5.6.5 Sex

Multiple studies have found that women are more likely to receive treatment for mental health difficulties than men[358–360] and it was hypothesised that this would also be true within our cohort of cancer survivors. Odds ratio of mental health services use is shown in table 5.9a and of mental health diagnosis on inpatient HES is shown in table 5.9b. Odds ratio of either mental health services use, mental health diagnosis or both is show in table 5.9c.

Table 5.9a Odds ratio of mental health services use for females compared to males[r]

Sex	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Male	4335	441	Reference		
Female	2918	336	1.15	0.99	1.34

[r] no additional model adjustment required

Table 5.9b Odds ratio of mental health diagnosis on inpatient Hospital Episode Statistics for females compared to males[s]

Sex	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
Male	4335	496	Reference		
Female	2918	409	1.26	1.10	1.45

Table 5.9c Odds ratio of mental health services use, mental health diagnosis on inpatient Hospital Episode Statistics or both for females compared to males[t]

Sex	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
Male	4335	740	Reference		
Female	2918	577	1.20	1.07	1.35

Female survivors were at a slightly increased risk of mental health services use compared to males, although the difference between males and females was not statistically significant. However, females were significantly more

[s] no additional model adjustment required

[t] no additional model adjustment required

likely to have a mental health diagnosis on inpatient HES. When both indicators of mental ill health were combined, females were at a significant higher risk than males of recorded mental ill health.

5.6.6 Stage at Diagnosis

It was hypothesised that individuals with higher, more advanced stage disease at diagnosis would be at greater risk of mental health services use. For individuals with non-CNS solid tumours, regression was performed to determine whether stage at diagnosis was associated with increased risk of mental health services use. For those with CNS tumours, where stage does not always apply, grade of tumour was investigated. For patients with leukaemia, white cell count at diagnosis (below or greater than 50) was explored. These results are shown in table 5.10a. Odds ratio of mental health diagnosis on inpatient HES is shown in table 5.10b. Odds ratio of one or both indicators of mental ill health is shown in table 5.10c.

Data on stage were only available for 1494 (33.1%) of the cohort with non-CNS solid tumours. Data on grade was available for all but 2 individuals with CNS tumours; the 2 individuals without available grade had morphology coded as “neoplasm of uncertain behaviour”, meaning it could not be. Data on presenting white cell count was available for 1250 (85.7%) of the cohort with leukaemia.

Table 5.10a Odds ratio of mental health services use for individuals with different stage or grade of disease at diagnosis[u]

Stage at diagnosis (non-CNS solid tumours)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
1	616	75	Reference		
2	500	58	0.99	0.67	1.46
3	175	14	0.77	0.41	1.42
4	205	22	1.19	0.70	2.02
Grade of tumour (CNS tumours)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Low (I-II)	1980	256	Reference		
High (III-IV)	882	78	0.63	0.43	0.92
White cell count at diagnosis (leukaemias)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	

[u] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, tumour type and year of diagnosis

<50	1024	87	Reference		
≥50	226	12	0.64	0.34	1.22

Table 5.10b Odds ratio of mental health diagnoses on inpatient Hospital Episode Statistics for individuals with different stage or grade of disease at diagnosis[v]

Stage at diagnosis (non-CNS solid tumours)	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
1	616	92	Reference		
2	500	73	0.97	0.69	1.38
3	175	23	0.95	0.57	1.57
4	205	21	0.80	0.48	1.35
Grade of tumour (CNS tumours)	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
Low (I-II)	1980	277	Reference		
High (III-IV)	882	90	0.82	0.56	1.19
White cell count at	Number of Individuals	Number with Mental Health	Odds ratio of Mental Health	95% Confidence Intervals	

[v] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, tumour type and year of diagnosis

diagnosis (leukaemias)		Diagnosis on Inpatient HES	Diagnosis on Inpatient HES		
<50	1024	99	Reference		
≥50	226	22	1.00	0.60	1.67

Table 5.10c Odds ratio of mental health services use, mental health diagnoses on inpatient Hospital Episode Statistics or both for individuals with different stage or grade of disease at diagnosis[w]

Stage at diagnosis (non-CNS solid tumours)	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
1	616	124	Reference		
2	500	101	1.02	0.75	1.38
3	175	33	1.05	0.68	1.62
4	205	34	1.01	0.90	1.41
Grade of tumour (CNS tumours)	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
Low (I-II)	1980	410	Reference		
High (III-IV)	882	134	0.65	0.47	0.90

[w] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, tumour type and year of diagnosis

White cell count at diagnosis (leukaemias)	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
<50	1024	154	Reference		
≥50	226	28	0.84	0.53	1.31

There was no significant difference in risk of mental health services use for any stage of tumour or high vs low white cell count at presentation. There did appear to be a reduced risk of mental health services use in those with stage 3 tumours (compared to stage 1 tumours), and in those with high grade CNS tumours (compared to low grade CNS tumours).

There was no significant difference in risk of mental health diagnosis on inpatient HES for any stage or grade of tumour or high vs low white cell count at presentation.

When both indicators of mental ill health (recorded mental health services contact and recorded mental health diagnosis on inpatient HES) were combined, those with high grade CNS tumours were at significantly reduced risk of recorded mental ill health compared to individuals with low grade tumours. Amongst individuals with a diagnosis of leukaemia or non-CNS solid tumours, white cell count at presentation and stage, respectively, had no impact on risk of recorded mental ill health.

Reasons for the increased risk of mental ill health amongst those with low grade CNS tumours are considered in the discussion, sections 7.2 Clinical Implications and 7.4.1 Discussion, Strengths and Limitations of the Mental Health Work.

5.6.7 Treatment at a Specialist Teenage Unit

As previously stated in section 1.3.2: Principal treatment centres for Teenagers and Young Adults, many 13-24 year olds are given the option of being treated in a specialist unit just for TYA patients. Given the positive

feedback these units have received, and the evidence that they result in improved outcomes[361], it was hypothesised that individuals treated on a specialist TYA unit would have reduced risk of mental health services use. As per the national guidance discussed in the thesis introduction, nearly all patients aged under 18 are treated in specialist units; this analysis was performed for patients aged 13-24, but also repeated just including those aged 18-24 at diagnosis. Given the lack of variation in place of treatment (specialist vs non-specialist units) for patients aged 13-17, this analysis was not felt to be worthwhile for this group specifically. Results are shown in Table 5.11a. Table 5.11b shows the results of similar calculations for the risk of mental health diagnoses on inpatient HES. Table 5.11c shows the results of the same logistic regression looking at either recorded mental health services use, recorded mental health diagnosis on inpatient HES, or both.

Table 5.11a Odds ratio of mental health services use for individuals treated on specialist TYA units compared to those treated on standard wards[x]

Treated in specialist TYA unit (age 13-24)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
No	759	86	Reference		
Yes	325	58	1.64	1.13	2.38
Treated in specialist TYA unit (age 18-24)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
No	547	63	Reference		
Yes	168	39	2.06	1.29	3.30

[x] adjusted for age at diagnosis, deprivation (Townsend deprivation index), sex, stage at diagnosis, treatment type (radiotherapy vs chemotherapy vs both vs neither), tumour type and year of diagnosis

Table 5.11b Odds ratio of mental health diagnosis on inpatient Hospital Episode Statistics for individuals treated on specialist TYA units compared to those treated on standard wards[y]

Treated in specialist TYA unit (age 13-24)	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
No	759	113	Reference		
Yes	325	62	1.29	0.90	1.83
Treated in specialist TYA unit (age 18-24)	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
No	547	84	Reference		
Yes	168	42	1.54	0.99	2.40

[y] adjusted for age at diagnosis, deprivation (Townsend deprivation index), sex, stage at diagnosis, treatment type (radiotherapy vs chemotherapy vs both vs neither), tumour type and year of diagnosis

Table 5.11c Odds ratio of mental health services use, recorded mental health diagnosis on inpatient Hospital Episode Statistics or both for individuals treated on specialist TYA units compared to those treated on standard wards[z]

Treated in specialist TYA unit (age 13-24)	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
No	759	164	Reference		
Yes	325	92	1.36	1.00	1.84
Treated in specialist TYA unit (age 18-24)	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
No	547	120	Reference		
Yes	168	62	1.78	1.20	2.64

There appeared to be an increased risk of mental health services use in patients treated on specialist TYA units. There also appeared to be an increased risk of mental health diagnosis on inpatient HES. When both indicators of mental ill health were combined, there appeared to be a greater risk of recorded mental health difficulties amongst individuals treated on specialist TYA units, and this association was stronger when only 18-24 year olds were considered. However, there was a lot of missing data in this field, i.e. it was unknown whether patients were treated in TYA units or not. Of

[z] adjusted for age at diagnosis, deprivation (Townsend deprivation index), sex, stage at diagnosis, treatment type (radiotherapy vs chemotherapy vs both vs neither), tumour type and year of diagnosis

2537 patients who were diagnosed between the ages of 13 and 24, data on place of treatment (TYA unit or otherwise) was missing for 1453. 583 of these were aged 13-17 at diagnosis, and 870 were aged 18-24. The analysis was therefore repeated for patients who were probably treated on a TYA unit; it was assumed that if a patient was treated in a centre with a specialist unit open at the time of their diagnosis, they received treatment there. The results of this analysis for mental health services use are shown in table 5.12a and for mental health diagnosis on inpatient HES are shown in table 5.12b. The results for combined indicators of mental ill health are shown in table 5.12c.

Table 5.12a Odds ratio of mental health services use for individuals probably treated on specialist TYA units compared to those probably treated on standard wards[aa]

Probably treated in specialist TYA unit (age 13-24)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
No	2045	256	Reference		
Yes	492	82	1.34	0.98	1.81
Probably treated in specialist TYA unit (age 18-24)	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
No	1364	172	Reference		
Yes	221	48	1.76	1.16	2.66

[aa] adjusted for age at diagnosis, deprivation (Townsend deprivation index), sex, stage at diagnosis, treatment type (radiotherapy vs chemotherapy vs both vs neither), tumour type and year of diagnosis

Table 5.12b Odds ratio of mental health diagnosis on inpatient Hospital Episode Statistics for individuals probably treated on specialist TYA units compared to those probably treated on standard wards[bb]

Probably treated in specialist TYA unit (age 13-24)	Number of Individuals	Number with Mental Health Diagnosis on inpatient HES	Odds ratio of Mental Health Diagnosis on inpatient HES	95% Confidence Intervals	
No	2045	300	Reference		
Yes	492	84	1.07	0.79	1.43
Probably treated in specialist TYA unit (age 18-24)	Number of Individuals	Number with Mental Health Diagnosis on inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
No	1364	212	Reference		
Yes	221	48	1.19	0.80	1.78

[bb] adjusted for age at diagnosis, deprivation (Townsend deprivation index), sex, stage at diagnosis, treatment type (radiotherapy vs chemotherapy vs both vs neither), tumour type and year of diagnosis

Table 5.12c Odds ratio of mental health services use, mental health diagnosis on inpatient Hospital Episode Statistics or both for individuals probably treated on specialist TYA units compared to those probably treated on standard wards[cc]

Probably treated in specialist TYA unit (age 13-24)	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
No	2045	440	Reference		
Yes	492	125	1.09	0.85	1.41
Probably treated in specialist TYA unit (age 18-24)	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
No	1364	302	Reference		
Yes	221	73	1.41	0.99	2.00

After including all patients who were likely to have been treated in specialist TYA units, there remained an increased risk of mental health services use amongst individuals aged 18-24 treated in specialist units, compared to those treated on standard units. A similar pattern was seen when all individuals aged 13-24 were included in the analysis, although this result did not achieve statistical significance. Risk of mental health diagnosis on inpatient HES did not appear to differ between individuals probably treated in specialist TYA units and those not treated on such units. When both indicators of mental ill health were combined, there was no difference in risk

[cc] adjusted for age at diagnosis, deprivation (Townsend deprivation index), sex, stage at diagnosis, treatment type (radiotherapy vs chemotherapy vs both vs neither), tumour type and year of diagnosis

of recorded mental ill health for 13-24 year olds probably treated on TYA units, although an increase in risk of recorded mental ill health for those aged 18-24 probably treated on specialist TYA units was suggested, although this did not achieve statistical significance. Reasons for the increased risk of specialist mental health services use in individuals treated on specialist TYA units are explored in section 7.4.1 Discussion, Strengths and Limitations of the Mental Health Work.

5.6.8 Treatment Type

It was hypothesised that different treatment types may impact likelihood of mental health service use. Logistic regression was used to determine whether having received chemotherapy, radiotherapy or both was associated with increased likelihood of mental health service use, or increased likelihood of mental health diagnosis on inpatient HES. It was also hypothesised that having undergone cranial irradiation would be a particular risk factor for the development of mental ill health. Individuals who had undergone radiotherapy and who had underlying diagnoses of either CNS tumours or leukaemias, were assumed to have undergone cranial irradiation. Risk of recorded mental health difficulties for those who had undergone cranial irradiation compared to those who hadn't was also explored. These results are shown in tables 5.13a and 5.13b, respectively. Table 5.13c shows the results for this regression looking at either mental health services use, mental health diagnosis on inpatient HES or both.

Table 5.13a Odds ratio of mental health services use for individuals treated with radiotherapy, combined chemo- and radiotherapy, and neither chemo- nor radiotherapy compared to those treated with chemotherapy only, and for individuals who had undergone cranial irradiation compared to those who hadn't[dd]

Treatment type	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Chemotherapy only	3634	364	Reference		
Radiotherapy only	297	30	0.77	0.51	1.15
Chemotherapy & radiotherapy	1147	99	0.84	0.66	1.08
Neither chemotherapy nor radiotherapy	2175	284	1.18	0.99	1.41
Treatment type	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
No cranial irradiation	6589	722	Reference		

[dd] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

Cranial irradiation	664	55	0.81	0.60	1.09

Table 5.13b Odds ratio of mental health diagnosis on inpatient Hospital Episode Statistics for individuals treated with radiotherapy, combined chemo- and radiotherapy, and neither chemo- nor radiotherapy compared to those treated with chemotherapy only, and for individuals who had undergone cranial irradiation compared to those who hadn't[ee]

Treatment type	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
Chemotherapy only	3634	459	Reference		
Radiotherapy only	297	43	0.92	0.65	1.30
Chemotherapy & radiotherapy	1147	105	0.75	0.59	0.94
Neither chemotherapy nor radiotherapy	2175	298	0.96	0.81	1.14
Treatment type	Number of Individuals	Number with Mental Health Diagnosis on	Odds ratio of Mental Health	95% Confidence Intervals	

[ee] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

		Inpatient HES	Diagnosis on Inpatient HES		
No cranial irradiation	6589	848	Reference		
Cranial irradiation	664	57	0.74	0.55	0.99

Table 5.13c Odds ratio of mental health services use, mental health diagnosis on inpatient Hospital Episode Statistics or both for individuals treated with radiotherapy, combined chemo- and radiotherapy, and neither chemo- nor radiotherapy compared to those treated with chemotherapy only, and for individuals who had undergone cranial irradiation compared to those who hadn't [ff]

Treatment type	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
Chemotherapy only	3634	654	Reference		
Radiotherapy only	297	59	0.88	0.65	1.20
Chemotherapy & radiotherapy	1147	161	0.78	0.64	0.95
Neither chemotherapy nor radiotherapy	2175	443	1.03	0.89	1.19

[ff] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

Treatment type	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
No cranial irradiation	6589	1229	Reference		
Cranial irradiation	664	88	0.75	0.59	0.96

Treatment with radiotherapy or combined chemotherapy and radiotherapy were not associated with increased risk of mental health services use compared with treatment with chemotherapy alone. However, treatment with neither chemotherapy nor radiotherapy was associated with increased risk of mental health services use compared with treatment with chemotherapy, although this result did not achieve statistical significance. Cranial irradiation was associated with a decreased risk of mental health services use, although this was not statistically significant. Treatment with combined chemo- and radiotherapy was associated with a significantly reduced risk of mental health diagnosis on inpatient HES compared to chemotherapy alone. There was no apparent difference in risk of mental health diagnosis on inpatient HES for patients treated with radiotherapy or neither chemo- nor radiotherapy. Individuals treated with cranial irradiation were significantly less likely to have a mental health diagnosis recorded on inpatient HES than individuals who hadn't received cranial irradiation.

When both indicators of mental ill health were combined, individuals who had received both chemo- and radiotherapy were at significantly decreased risk of recorded mental ill health compared to those who had only received chemotherapy. Individuals who had been treated with cranial irradiation were at significantly decreased risk of recorded mental ill health compared to those who had not received cranial irradiation.

It was not immediately clear why individuals who had not received either chemotherapy or radiotherapy would be at increased risk of mental health

services use or risk of mental health diagnosis on inpatient HES. It was hypothesised that many of the individuals who had not received either chemotherapy or radiotherapy had had low grade CNS tumours which were treated with surgical resection alone. These individuals may have significant residual disability, placing them at high risk of mental health difficulties. In order to test this hypothesis, the regression looking at treatment type was performed separately for individuals with CNS tumours and other diagnoses. The results of these regressions are shown in tables 5.13d, 5.13e and 5.13f.

Table 5.13d Odds ratio of mental health services use for individuals treated with chemotherapy, radiotherapy and combined chemo- and radiotherapy, compared to those treated with and neither chemo- nor radiotherapy, for individuals with CNS tumours; and odds ratio of mental health services use for individuals treated with radiotherapy, combined chemo- and radiotherapy, and neither chemo- nor radiotherapy compared to those treated with chemotherapy only, for individuals with other diagnoses [gg]

Treatment type	Number of Individuals	Number with Mental Health Services Use	RR of Mental Health Services Use	95% Confidence Intervals	
CNS tumours					
Neither chemotherapy nor radiotherapy	635	102	Reference		
Chemotherapy only	271	27	0.67	0.41	1.08

[gg] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

Radiotherapy only	83	7	0.46	0.20	1.05
Chemotherapy & radiotherapy	290	25	0.54	0.32	0.91
Diagnoses other than CNS tumours					
Neither chemotherapy nor radiotherapy	1540	182	0.98	0.79	1.21
Chemotherapy only	3363	337	Reference		
Radiotherapy only	214	23	0.78	0.49	1.24
Chemotherapy & radiotherapy	857	74	0.85	0.65	1.12

Table 5.13e Odds ratio of mental health diagnosis on inpatient Hospital Episode Statistics for individuals treated with chemotherapy, radiotherapy and combined chemo- and radiotherapy, compared to those treated with and neither chemo- nor radiotherapy, for individuals with CNS tumours; and odds ratio of mental health services use for individuals treated with radiotherapy, combined chemo- and radiotherapy, and neither chemo- nor radiotherapy compared to those treated with chemotherapy only, for individuals with other diagnoses [hh]

Treatment type	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
CNS tumours					
Neither chemotherapy nor radiotherapy	635	94	Reference		
Chemotherapy only	271	30	0.97	0.60	1.57
Radiotherapy only	83	10	0.75	0.37	1.54
Chemotherapy & radiotherapy	290	22	0.66	0.38	1.14
Diagnoses other than CNS tumours					
Neither chemotherapy	1540	204	0.87	0.71	1.06

[hh] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

nor radiotherapy					
Chemotherapy only	3363	429	Reference		
Radiotherapy only	214	33	0.93	0.63	1.39
Chemotherapy & radiotherapy	857	83	0.75	0.58	0.97

Table 5.13f Odds ratio of mental health services use, mental health diagnosis on inpatient Hospital Episode Statistics, or both for individuals treated with chemotherapy, radiotherapy and combined chemo- and radiotherapy, compared to those treated with and neither chemo- nor radiotherapy, for individuals with CNS tumours; and odds ratio of mental health services use for individuals treated with radiotherapy, combined chemo- and radiotherapy, and neither chemo- nor radiotherapy compared to those treated with chemotherapy only, for individuals with other diagnoses [ii]

Treatment type	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals
CNS tumours				
Neither chemotherapy nor radiotherapy	635	156	Reference	

[ii] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

Chemotherapy only	271	42	0.72	0.48	1.07
Radiotherapy only	83	14	0.61	0.33	1.14
Chemotherapy & radiotherapy	290	34	0.54	0.34	0.84
Diagnoses other than CNS tumours					
Neither chemotherapy nor radiotherapy	1540	287	0.85	0.71	1.00
Chemotherapy only	3363	612	Reference		
Radiotherapy only	214	45	0.89	0.62	1.26
Chemotherapy & radiotherapy	857	127	0.79	0.64	0.99

Amongst individuals with CNS tumours, those treated with both chemo- and radiotherapy had significantly lower risk of mental health services use than those treated with neither chemo- nor radiotherapy. Amongst individuals with other diagnoses, no particular treatment type appeared to be associated with increased risk of mental health services use.

Individuals with diagnoses other than CNS tumours treated with both chemo- and radiotherapy had significantly lower risk of mental health diagnoses on inpatient HES than those treated with chemotherapy alone. Individuals with CNS tumours did not appear to be at any particular risk of mental health diagnoses on inpatient HES based upon treatment type.

When both indicators of mental ill health were combined, individuals who had received both chemo- and radiotherapy were at significantly decreased risk of recorded mental ill health in both the CNS and non-CNS groups. The

increased risk of recorded mental ill health in individuals treated with neither chemotherapy nor radiotherapy was no longer seen when CNS tumours and other diagnoses were looked at separately.

5.6.9 National Cancer Survivor Initiative Levels

Whilst it was possible to compare the risks of mental health service use between patients who had received different treatment modalities, this did not take into account the intensity of these treatments. However, NCSI levels are based on treatment intensity and are thus a proxy marker for intensity of treatment. Logistic regression was carried out to determine the likelihood of having a contact with specialist mental health services, a documented mental health co-morbidity, or both, depending on NCSI level. It was hypothesised that individuals allocated NCSI level 3, who had undergone the most intensive treatment, would be at greatest risk of mental health services use and mental health co-morbidity. Odds ratio of specialist mental health services use, of recorded mental health diagnosis on inpatient HES, and both, are shown in tables 5.14a, 5.14b and 5.14c, respectively.

Table 5.14a Odds ratio of specialist mental health services use for individuals allocated different National Cancer Survivor Initiative Levels[jj]

National Cancer Survivor Initiative Level	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals
1	64	7	1.21	0.52-2.80
2	1018	77	Reference	
3	427	64	1.84	1.26-2.70

[jj] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

Table 5.14b Odds ratio of recorded mental health diagnoses on inpatient Hospital Episode Statistics for individuals allocated different National Cancer Survivor Initiative Levels[kk]

National Cancer Survivor Initiative Level	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals
1	64	7	1.36	0.59-3.14
2	1018	76	Reference	
3	427	69	2.31	1.59-3.36

Table 5.14c Odds ratio of specialist mental health services use, recorded mental health diagnoses on inpatient Hospital Episode Statistics, or both for individuals allocated different National Cancer Survivor Initiative Levels[ll]

National Cancer Survivor Initiative Level	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals
1	64	10	1.18	0.58-2.42
2	1018	120	Reference	
3	427	109	2.39	1.74-3.25

Individuals allocated an NCSI level of 3 appeared to be at twice the risk of mental ill health than those allocated a level of 2. Those allocated a level of

[kk] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

[ll] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

1 appeared to be at a slight increased risk of mental ill health than those allocated a level of 2, although this difference was not statistically significant.

It was hypothesised that a number of the individuals allocated NCSI level 3 would be survivors of high-grade CNS tumours, and that those individuals may have different risks of mental health difficulties. Therefore, the regression looking at NCSI was performed separately for individuals with CNS tumours and other diagnoses. The results of these regressions are shown in tables 5.14d, 5.14e and 5.14f.

Table 5.14d Odds ratio of specialist mental health services use for individuals allocated different National Cancer Survivor Initiative Levels, for individuals with CNS tumours and other diagnoses[mm]

National Cancer Survivor Initiative Level	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals
CNS Tumours				
1	4	0	No cases on MH register	
2	120	3	Reference	
3	114	24	4.00	0.78-20.45
Diagnoses other than CNS tumours				
1	60	7	1.23	0.51-2.95
2	898	74	Reference	
3	313	40	1.51	0.99-2.31

[mm] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

Table 5.14e Odds ratio of mental health diagnoses on inpatient Hospital Episode Statistics for individuals allocated different National Cancer Survivor Initiative Levels, for individuals with CNS tumours and other diagnoses[nn]

National Cancer Survivor Initiative Level	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals
CNS Tumours				
1	4	0	No cases on MH register	
2	120	1	Reference	
3	114	19	24.10	2.02-287.72
Diagnoses other than CNS tumours				
1	60	7	1.10	0.47-2.63
2	898	75	Reference	
3	313	50	1.88	1.26-2.80

[nn] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

Table 5.14f Odds ratio of recorded specialist mental health services use, mental health diagnoses on inpatient Hospital Episode Statistics, or both, for individuals allocated different National Cancer Survivor Initiative Levels, for individuals with CNS tumours and other diagnoses[oo]

National Cancer Survivor Initiative Level	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals
CNS Tumours				
1	4	0	No cases on MH register	
2	120	4	Reference	
3	114	33	4.62	1.10-19.35
Diagnoses other than CNS tumours				
1	60	10	1.11	0.53-2.33
2	898	116	Reference	
3	313	76	2.00	1.43-2.81

Due to smaller numbers, it was not possible to draw conclusions about the risks of mental ill health for individuals who had had a diagnosis of CNS tumour and were allocated NCSI level 1. However, the risk of recorded mental ill health, and particularly recorded mental health conditions on inpatient HES, was significantly greater amongst CNS tumour survivors allocated NCSI level 3 than level 2.

Amongst individuals with diagnoses other than CNS tumours, those with NCSI level 3 were twice as likely to have recorded mental ill health as those with NCSI level 2. Individuals with NCSI level 1 appeared slightly more likely

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[oo] adjusted for age at diagnosis, stage at diagnosis, tumour type and year of diagnosis

than those with level 2 to have recorded mental ill health, however this result was not statistically significant.

5.6.10 Tumour Type

As different tumour types have different treatments, prognoses and risks of late effects, it was hypothesised that different tumour types would be associated with different risks of mental health service use. Due to comparatively small numbers of individuals with diagnoses of neuroblastoma, retinoblastoma, renal tumours, liver tumours, bone tumours, soft tissue sarcomas, other epithelial tumours and miscellaneous tumours, these diagnoses were all grouped together as “non-CNS, non-germ cell solid tumours”. This was based on the ICCC criteria, however the largest groups of leukaemia, lymphoma, CNS tumours and germ cell tumours were the same in both Birch and ICCC criteria. Due to hypothesised differences between survivors of high and low grade CNS tumours, these were considered separately. Data on tumour type were available for all individuals, although of 1279 individuals with CNS tumours, grade was missing for 2. The results of the logistic regression on tumour type are show in table 5.15a. The regression was repeated looking at Odds ratio of mental health diagnosis on inpatient HES and these results are shown in table 5.15b. Finally, the regression was carried out a third time for combined risks of mental health service use, mental health diagnosis on inpatient HES, or both, and these results are presented in table 5.15c.

Table 5.15a Odds ratio of mental health services use for individuals with diagnoses of leukaemia, lymphoma, CNS tumour and germ cell tumour compared to non-CNS, non-germ cell tumours. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[pp]

Diagnosis	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Non-CNS, non-germ cell solid tumour	1946	193	Reference		
Leukaemia	1454	116	0.91	0.71	1.17
Lymphoma	1420	166	1.08	0.86	1.36
Low grade CNS tumour	863	123	1.54	1.20	1.97
High grade CNS tumour	425	38	0.98	0.68	1.42
Germ cell tumour	1143	141	1.13	0.88	1.46

[pp] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

Table 5.15b Odds ratio of mental health diagnosis on inpatient Hospital Episode Statistics for individuals with diagnoses of leukaemia, lymphoma, CNS tumour and germ cell tumour compared to non-CNS, non-germ cell tumours. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[qq]

Diagnosis	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
Non-CNS, non-germ cell solid tumour	1946	232	Reference		
Leukaemia	1454	141	0.91	0.73	1.14
Lymphoma	1420	213	1.15	0.94	1.42
Low grade CNS tumour	863	112	1.11	0.87	1.42
High grade CNS tumour	425	44	0.92	0.65	1.30
Germ cell tumour	1143	163	1.11	0.88	1.40

[qq] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

Table 5.15c Odds ratio of recorded mental health services use, mental health diagnosis on inpatient Hospital Episode Statistics or both for individuals with diagnoses of leukaemia, lymphoma, CNS tumour and germ cell tumour compared to non-CNS, non-germ cell tumours. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[rr]

Diagnosis	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
Non-CNS, non-germ cell solid tumour	1946	334	Reference		
Leukaemia	1454	209	0.93	0.77	1.13
Lymphoma	1420	298	1.14	0.95	1.36
Low grade CNS tumour	863	185	1.33	1.08	1.63
High grade CNS tumour	425	61	0.88	0.65	1.19
Germ cell tumour	1143	230	1.07	0.87	1.32

Only low grade CNS tumours were associated with a significantly increased risk of mental health services use compared to non-CNS non-germ cell solid tumours (RR 1.33, 95% CI 1.08-1.63). High grade CNS tumours appeared to have a lower risk of mental health services use compared to non-CNS non-germ cell solid tumours. No tumour group was associated with a notably increased risk of mental health diagnosis on inpatient HES.

[rr] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

When both indicators of mental ill health were considered, those with low grade CNS tumours appeared to be at an increased risk of recorded mental ill health compared to non-CNS non-germ cell solid tumours. No other diagnostic group appeared to be at increased risk of recorded mental ill health, although high grade CNS tumours appeared to be associated with a decreased risk of recorded mental ill health.

Given that the ICCC and Birch classifications were specifically designed for particular age groups, the analysis was run separately for children (0-14) using the ICCC and for TYA (15-29) using the Birch system. Tables 5.15d, 5.15e and 5.15f show the results for children based on the ICCC and tables 5.15g, 5.15h and 5.15i show the results for TYA based on the Birch system.

Table 5.15d Odds ratio of mental health services use for individuals with different diagnoses, compared to those with leukaemia, for individuals aged 0-14 at diagnosis. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[ss]

Diagnosis	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Leukaemia	1104	75	Reference		
Lymphoma	437	36	1.10	0.72	1.70
Low grade CNS tumour	532	65	1.79	1.25	2.56
High grade CNS tumour	295	25	1.27	0.79	2.04
Neuroblastoma	215	12	0.88	0.47	1.67
Retinoblastoma	124	9	1.26	0.60	2.62

[ss] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

Renal tumour	209	15	1.15	0.64	2.06
Liver tumour	32	0	No cases on MH register		
Bone tumour	157	13	1.07	0.57	2.02
Soft tissue sarcoma	238	20	1.24	0.74	2.09
Germ cell tumour	138	11	1.18	0.61	2.29
Miscellaneous/other	66	2	0.41	0.10	1.72

Table 5.15e Odds ratio of recorded mental health diagnoses on inpatient Hospital Episode Statistics for individuals with different diagnoses, compared to those with leukaemia, for individuals aged 0-14 at diagnosis. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[tt]

Diagnosis	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Leukaemia	1104	86	Reference		
Lymphoma	437	53	1.53	1.05	2.24
Low grade CNS tumour	532	57	1.32	0.92	1.89
High grade CNS tumour	295	23	0.99	0.61	1.60
Neuroblastoma	215	12	0.75	0.40	1.41
Retinoblastoma	124	9	1.08	0.52	2.23
Renal tumour	209	24	1.62	0.99	2.63
Liver tumour	32	1	0.39	0.05	2.92
Bone tumour	157	21	1.64	0.96	2.78
Soft tissue sarcoma	238	21	1.11	0.67	1.83
Germ cell tumour	138	15	1.35	0.76	2.43
Miscellaneous/other	66	2	0.34	0.08	1.41

[tt] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

Table 5.15f Odds ratio of recorded mental ill health for individuals with different diagnoses, compared to those with leukaemia, for individuals aged 0-14 at diagnosis. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[uu]

Diagnosis	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Leukaemia	1104	136	Reference		
Lymphoma	437	72	1.27	0.92	1.76
Low grade CNS tumour	532	95	1.43	1.07	1.92
High grade CNS tumour	295	36	0.98	0.66	1.45
Neuroblastoma	215	20	0.79	0.48	1.31
Retinoblastoma	124	15	1.16	0.65	2.08
Renal tumour	209	29	1.23	0.80	1.91
Liver tumour	32	1	0.25	0.03	1.83
Bone tumour	157	29	1.41	0.89	2.23
Soft tissue sarcoma	238	34	1.15	0.76	1.73
Germ cell tumour	138	21	1.23	0.74	2.03
Miscellaneous/other	66	3	0.31	0.10	1.01

[uu] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

Table 5.15g Odds ratio of mental health services use for individuals with different diagnoses, compared to those with leukaemia, for individuals aged 15-29 at diagnosis. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[vv]

Diagnosis	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Leukaemia	349	41	0.76	0.51	1.13
Lymphoma	973	128	0.88	0.66	1.18
Low grade CNS tumour	330	58	1.22	0.85	1.75
High grade CNS tumour	130	13	0.64	0.35	1.19
Bone tumour	163	20	0.82	0.48	1.37
Soft tissue sarcoma	177	25	1.00	0.62	1.62
Germ cell tumour	989	127	Reference		
Melanoma/skin cancer	18	1	0.32	0.04	2.49
Carcinoma	537	73	0.85	0.59	1.21
Miscellaneous/other	38	8	1.59	0.70	3.61

[vv] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

Table 5.15h Odds ratio of recorded mental health diagnoses on inpatient Hospital Episode Statistics for individuals with different diagnoses, compared to those with leukaemia, for individuals aged 15-29 at diagnosis. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[ww]

Diagnosis	Number of Individuals	Number with Mental Health Diagnosis on Inpatient HES	Odds ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
Leukaemia	349	55	0.92	0.64	1.31
Lymphoma	973	159	1.00	0.77	1.30
Low grade CNS tumour	330	55	1.00	0.70	1.43
High grade CNS tumour	130	21	0.95	0.57	1.58
Bone tumour	163	23	0.82	0.50	1.34
Soft tissue sarcoma	177	28	0.98	0.62	1.55
Germ cell tumour	989	144	Reference		
Melanoma/skin cancer	18	3	0.95	0.27	3.41
Carcinoma	537	85	0.96	0.70	1.34
Miscellaneous/other	38	8	1.35	0.59	3.08

[ww] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

Table 5.15i Odds ratio of mental health services use, recorded mental health diagnosis on inpatient Hospital Episode Statistics or both, for individuals with different diagnoses, compared to those with leukaemia, for individuals aged 15-29 at diagnosis. CNS tumours are divided into low (grades 1-2) and high (grades 3-4) grade tumours[xx]

Diagnosis	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals	
Leukaemia	349	73	0.85	0.62	1.17
Lymphoma	973	223	0.99	0.79	1.25
Low grade CNS tumour	330	90	1.23	0.90	1.67
High grade CNS tumour	130	25	0.77	0.48	1.24
Bone tumour	163	33	0.83	0.54	1.28
Soft tissue sarcoma	177	43	1.13	0.76	1.68
Germ cell tumour	989	204	Reference		
Melanoma/skin cancer	18	3	0.63	0.18	2.23
Carcinoma	537	120	0.93	0.69	1.24
Miscellaneous/other	38	12	1.57	0.76	3.24

Amongst individuals diagnosed under the age of 15, those with a low grade brain tumour were associated with over twice the risk of specialist mental health services use compared to those diagnosed with leukaemia. Amongst

[xx] adjusted for age at diagnosis, deprivation (Townsend deprivation index), ethnicity, sex and year of diagnosis

those diagnosed during the TYA period, an increased risk of specialist mental health services use was also seen for those with low grade brain tumours when compared to germ cell tumours. No other diagnoses were associated with a clinically significantly different risk of specialist mental health services use.

When considering risk of recorded mental health diagnosis on inpatient HES, amongst those diagnosed aged 0-14, renal tumours were the only diagnostic group associated with increased risk of mental health diagnosis compared to leukaemias. There was no difference in risk of having a recorded mental health diagnosis on inpatient HES between different diagnostic groups for those diagnosed aged 15-29.

When both indicators of mental ill health were considered together, low grade CNS tumours were associated with an increased risk of recorded mental ill health compared to leukaemias amongst those diagnosed under the age of 15. Amongst those diagnosed in the TYA period, no particular diagnostic group was associated with a marked increased risk of recorded mental ill health when compared to germ cell tumours, although low grade CNS tumours tended toward significance with a lower confidence interval approaching 1 (RR 1.23; 95% CI 0.96-1.67).

5.6.11 Year of Diagnosis

Given that treatments have changed over the years, and also that, as more time post-diagnosis elapses, people's perceptions and thoughts regarding their cancer may change, it was hypothesised that year of diagnosis would potentially impact risk of mental health services use and risk of mental health diagnosis on inpatient HES. The results of the regression analysis for year of diagnosis are shown in tables 5.16a, 5.16b and 5.16c according to age group at diagnosis.

Table 5.16a Odds ratio of mental health services use for individuals diagnosed in different periods, compared to those diagnosed between 2005 and 2009, for children (0-14), teenagers and young adults (15-29) and all patients (0-29)[yy]

Diagnosis period	Number of Individuals	Number with Mental Health Services Use	Odds ratio of Mental Health Services Use	95% Confidence Intervals	
Children (0-14)					
1974-1979	403	29	2.01	1.14	3.56
1980-1984	326	31	2.72	1.55	4.92
1985-1989	386	47	3.59	2.13	6.07
1990-1994	449	53	3.47	2.08	5.79
1995-1999	468	43	2.62	1.54	4.45
2000-2004	607	51	2.38	1.42	3.97
2005-2009	592	22	Reference		
2010-2012	318	7	0.58	0.25	1.38
Teenagers and young adults (15-29)					
1990-1994	590	63	0.68	0.50	0.93

[yy] no additional model adjustment required

1995-1999	711	86	0.79	0.59	1.04
2000-2004	898	112	0.82	0.63	1.06
2005-2009	1049	156	Reference		
2010-2012	455	77	1.17	0.87	1.57
All individuals (0-29)					
1990-1994	1039	116	1.03	0.81	1.32
1995-1999	1179	129	1.01	0.79	1.28
2000-2004	1505	163	1.00	0.80	1.25
2005-2009	1641	178	Reference		
2010-2012	773	84	1.00	0.76	1.32

Table 5.16b Odds ratio of mental health diagnosis on inpatient Hospital Episode Statistics for individuals diagnosed in different periods, compared to those diagnosed between 2005 and 2009, for children (0-14), teenagers and young adults (15-29) and all patients (0-29)[zz]

Diagnosis period	Number of Individuals	Number with Mental Health	Odds ratio of Mental Health	95% Confidence Intervals

[zz] no additional model adjustment required

		Diagnosis on Inpatient HES	Diagnosis on Inpatient HES		
Children (0-14)					
1974-1979	403	31	1.56	0.93	2.63
1980-1984	326	32	2.04	1.22	3.42
1985-1989	386	44	2.41	1.49	3.91
1990-1994	449	49	2.29	1.43	3.68
1995-1999	468	54	2.44	1.54	3.89
2000-2004	607	60	2.05	1.31	3.23
2005-2009	704	30	Reference		
2010-2012	206	24	1.53	0.88	2.66
Teenagers and young adults (15-29)					
1990-1994	590	67	0.70	0.52	0.95
1995-1999	711	99	0.89	0.68	1.16
2000-2004	898	163	1.21	0.96	1.54

2005-2009	1049	162	Reference		
2010-2012	455	90	1.35	1.02	1.80
All individuals (0-29)					
1990-1994	1039	116	0.95	0.74	1.21
1995-1999	1179	153	1.13	0.90	1.41
2000-2004	1505	223	1.31	1.07	1.61
2005-2009	1641	192	Reference		
2010-2012	773	114	1.31	1.02	1.68

Table 5.16c Odds ratio of mental health services use, mental health diagnosis on inpatient Hospital Episode Statistics or both for individuals diagnosed in different periods, compared to those diagnosed between 2005 and 2009, for children (0-14), TYA (15-29) and all patients (0-29)[aaa]

Diagnosis period	Number of Individuals	Number with Recorded Mental Ill Health	Odds ratio of Recorded Mental Ill Health	95% Confidence Intervals
Children (0-14)				

[aaa] no additional model adjustment required

1974-1979	403	47	1.64	1.07	2.53
1980-1984	326	47	2.10	1.36	3.24
1985-1989	386	73	2.90	1.95	4.33
1990-1994	449	78	2.62	1.77	3.88
1995-1999	468	81	2.61	1.77	3.85
2000-2004	607	93	2.25	1.54	3.29
2005-2009	592	44	Reference		
2010-2012	318	28	1.20	0.73	1.97
Teenagers and young adults (15-29)					
1990-1994	590	104	0.70	0.54	0.90
1995-1999	711	140	0.80	0.63	1.01
2000-2004	898	205	0.97	0.78	1.19
2005-2009	1049	246	Reference		
2010-2012	455	131	1.32	1.03	1.69

All individuals (0-29)					
1990-1994	1039	182	0.99	0.81	1.21
1995-1999	1179	221	1.07	0.89	1.30
2000-2004	1505	298	1.15	0.96	1.38
2005-2009	1641	290	Reference		
2010-2012	773	159	1.21	0.97	1.50

The risk of mental health services contact for those diagnosed under the age of 15 was higher in those individuals diagnosed before 2005, and appeared slightly lower in those diagnosed after 2009. A similar pattern was seen for risk of mental health diagnosis on inpatient HES, with this being increased for all time periods of diagnosis aside from 1974-1979. In those who were aged 15-29 at diagnosis, there was a lower risk of mental health services contact for those diagnosed before 2005, although this was only statistically significant for the year group 1990-1994 (RR 0.70; 95% CI 0.54-0.90). Risk of mental health diagnosis on inpatient HES appeared lower for those diagnosed in 1990-1994 and 1995-1999 but slightly higher for those diagnosed in 2000-2004 and 2010-2012. When all age groups were combined, only those diagnosed in the period 1974-1979 were at lower risk than those diagnosed in 2005-2009. The only clear difference in risk of mental health diagnosis on inpatient HES was for those diagnosed in 2000-2004 and 2010-2012, who appeared at higher risk than those diagnosed in 2005-2009.

When both indicators of mental ill health were considered together, taking all children and young people together as one group, there was a reduced risk of recorded mental health contact in those diagnosed in 1974-1979, but no

other period. However, when children diagnosed aged 14 or under were considered separately, they had greater risk of recorded mental ill health if they were diagnosed before 2005, with this risk appearing greatest for those diagnosed in 1985-1989. Young people aged 15 and over at diagnosis had increased risk of recorded mental ill health if they were diagnosed after 2009.

Chapter 6 The Impact of Fertility Preservation on Mental Health

6.1 Introduction

As described in the introduction to this thesis, subfertility is a common LE of CYP's cancer[112], and one which is associated strongly with poor mental health[142]. Subfertility can be a considerable cause of distress and is associated with difficulties with romantic relationships as well as the direct impact on the likelihood of having children. Subfertility amongst cancer survivors may have a causative link to mental health disorders[142].

In male cancer patients, cryopreservation of semen samples prior to beginning anti-cancer therapy is the only reliable fertility preservation strategy available, however this has been shown to be feasible even in young pubertal patients[362]. For pre-pubertal patients, there are no proven fertility preservation strategies, although with advances in technology it may become possible in the future to preserve testicular tissue for this purpose[363].

Subfertility can be extremely distressing and the link between subfertility and mental ill health is well documented[364]. There have been suggestions that mental health professionals have a role to play in the management of subfertility[365]. Within the UK, it is a requirement that any licensed centre providing assisted reproductive therapies employs a trained counsellor, but more expert roles are not required[366].

There have been small studies assessing the impact of fertility preservation on mental distress in cancer patients, but these have almost exclusively focussed on females[367]. One small study suggested that fertility preservation was beneficial in reducing distress related to subfertility, but only 9 males were included[368].

This work aimed to determine:

- the rate of semen cryopreservation amongst male patients with a record on the YSRCCYP
- the percentage of male patients with normal vs subfertility following cancer treatment

- whether having undergone fertility preservation impacted risk of inclusion on the MHMDS or recorded mental health diagnosis on inpatient HES
- whether subfertility impacted risk of inclusion on the MHMDS/MHLDDS or recorded mental health diagnosis on inpatient HES

6.1.1 Hypotheses

It was hypothesised that

- having undergone semen cryopreservation would be associated with reduced risk of inclusion on the MHMDS/MHLDDS or recorded mental health diagnosis on inpatient HES
- subfertility following cancer treatment would be associated with increased risk of inclusion on the MHMDS/MHLDDS or recorded mental health diagnosis on inpatient HES.

6.2 Methods

As described in the methods section, a list of patients who had undergone semen cryopreservation for a diagnosis of malignant disease was obtained from our local fertility service and a retrospective case note review was carried out.

We had details of all patients who had banked semen since 2008. This included patients of all age groups and for a variety of indications, not just a cancer diagnosis.

In order to be included in this analysis, patients had to have a co-existing record on the YSRCCYP, meaning they were storing semen due to a diagnosis of cancer, and their cancer diagnosis was made at the age of 29 years or younger.

Data were extracted from paper fertility clinic notes by 2 individuals, who worked together to create an electronic form containing all relevant information. Data were gathered on the patient's age at banking, indication for banking (i.e. their underlying diagnosis), paternity status at banking, the number of ampoules of semen banked and semen analysis at the time of banking. Information was also recorded regarding whether a patient had ever returned to the fertility clinic, whether they had undergone any assisted reproductive techniques and, if so, the outcome of these techniques.

Electronic patient records on the PPM+ system (the system used by LTHT) contain details of clinic appointments, correspondence and investigations for the majority of clinical specialties, including oncology and haematology for patients of all ages. Full electronic records were only accessible for those patients who had been treated in Leeds Teaching Hospitals NHS Trust. In this cohort, this was 30.8% of the patients initially identified, and 75.5% of those who had banked semen. Review of the PPM+ records allowed the malignant diagnosis recorded in the fertility notes and the YSRCCYP to be verified. Data were also gathered regarding whether patients had continued to be seen in the haematology or oncology clinic.

Data on semen cryopreservation was linked to the working extract from the YSRCCYP to identify patients who were both 5 year survivors of CYP's cancer and who had undergone semen cryopreservation.

Patients on the YSRCCYP who were male diagnosed with cancer in 2008 or later and who were 13 or older at the time of diagnosis, but who had not undergone semen cryopreservation, were identified as controls. As there are multiple potential fertility services within the Yorkshire areas, only patients who were likely to have stored semen at Leeds Fertility (those from Bradford, Wakefield, Airedale, Harrogate, Leeds, Halifax, Huddersfield and Harrogate) were included as controls. Data on which cancer diagnoses patients had, as well as their age at diagnosis and year of diagnosis, were ascertained directly from the YSRCCYP and used to verify the data collected from the fertility records.

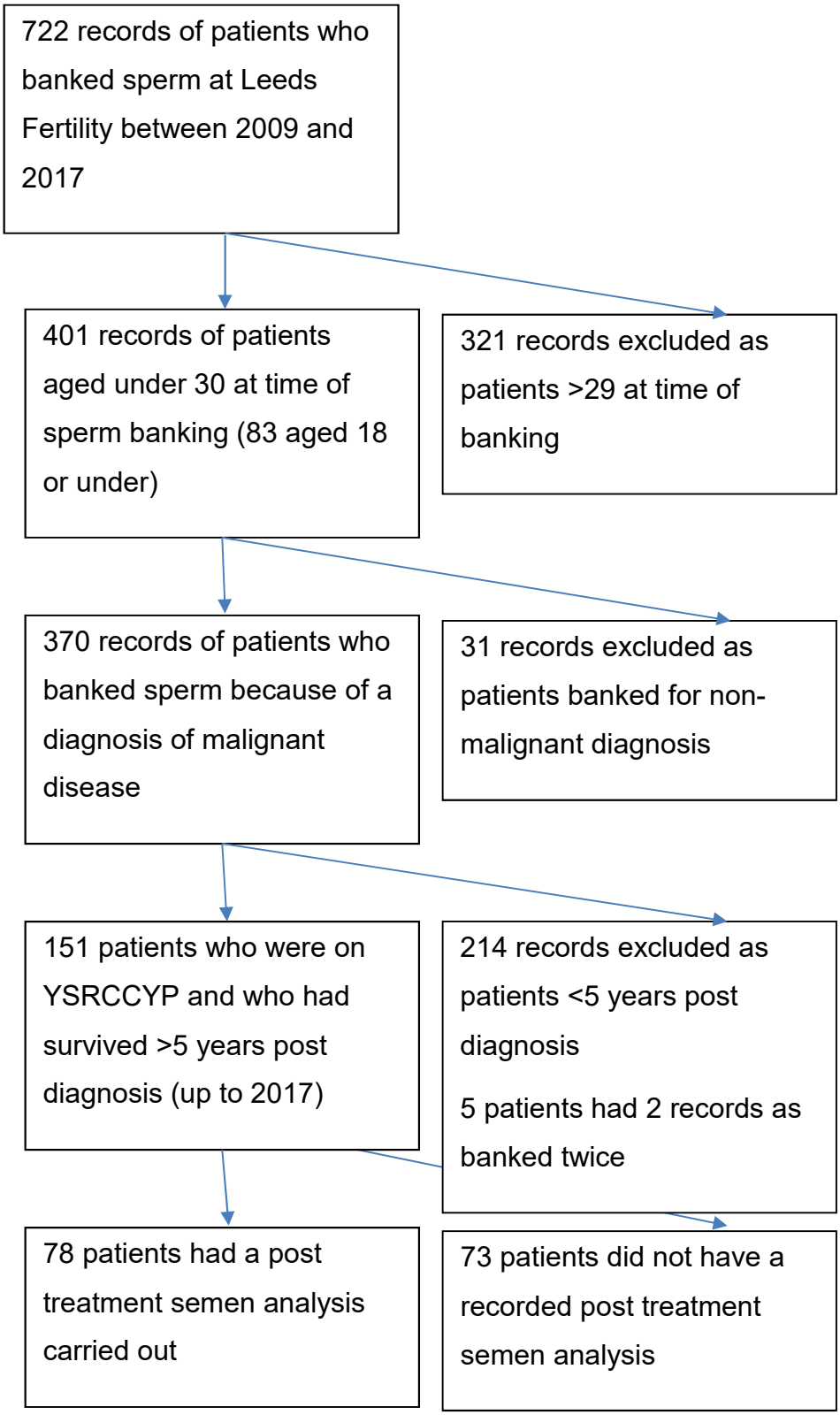
As described in the methods chapter, the MHMDS and MHLDDS, as well as the inpatient dataset, were used to identify patients who had used specialist mental health services, and the inpatient dataset was used to identify patients with mental health diagnoses.

6.3 Results

A total of 363 patients on the working YSRCCYP extract were males diagnosed with cancer in 2008 or later who were 13 or older at diagnosis and who were from regions likely to bank semen at Leeds Fertility.

722 fertility records were provided Leeds Fertility. From these, we identified 151 patients who had a record on the YSRCCYP and who had survived more than 5 years post diagnosis. The consort diagram shown in figure 6.1 gives the reasons for excluding other records.

Figure 6.1 Consort diagram showing patients who had banked semen for cryopreservation prior to cancer treatment and who had a record on the YSRCCYP



This meant there were data available on 151 patients who had banked semen and 212 controls, and that 41.6% of the eligible population (i.e. 151 out of an eligible 363) had undergone semen cryopreservation.

Characteristics of those eligible to bank sperm, those who did and those who didn't have a sample stored are summarised in Tables 6.1a-6.1d.

Table 6.1a Age at diagnosis of malignancy of patients who did and didn't undergo semen cryopreservation[bbb]

Characteristic	Eligible to Bank	Banked Sample (%)	Didn't Bank Sample (%)	χ^2 Statistic (p value)[ccc]
Age group at diagnosis				
13-17	82	25 (30.5%)	57 (69.5%)	5.09 (0.02)*
18-29	279	124 (44.4%)	155 (55.6%)	
Total	361	149 (41.3%)	212 (58.7%)	

[bbb] There were also 2 patients aged 3 and 11, respectively, at the time of initial cancer diagnosis who banked after a diagnosis of relapse or second malignancy.

[ccc] *denotes statistical significance

Table 6.1b Characteristics of patients who did and didn't undergo semen cryopreservation who were aged between 13 and 17 at the time of diagnosis of malignancy

Characteristic	Eligible to Bank	Banked Sample (%)	Didn't Bank Sample (%)	P value[ddd]
Tumour Group				
Leukaemia	21	7 (33.3%)	14 (66.7%)	0.10
Lymphoma	19	8 (42.1%)	11 (57.9%)	
CNS	19	1 (5.3%)	18 (94.7%)	
Germ Cell	8	3 (37.5%)	5 (62.5%)	
Non CNS solid	15	6 (40%)	9 (60%)	
Deprivation fifth				
1	22	12 (54.5%)	10 (45.5%)	0.07
2	13	3 (23.1%)	10 (76.9%)	
3	12	1 (8.3%)	11 (91.7%)	
4	19	7 (36.8%)	12 (63.2%)	
5	16	7 (43.8%)	9 (56.3%)	
Ethnic Group				
White	69	21 (30.4%)	48 (69.6%)	0.593
South Asian	7	3 (42.9%)	4 (57.1%)	
Other	6	1 (16.7%)	5 (83.3%)	

[ddd] *denotes statistical significance

Table 6.1c Characteristics of patients who did and didn't undergo semen cryopreservation who were aged between 18 and 29 at the time of diagnosis of malignancy

Characteristic	Eligible to Bank	Banked Sample	Didn't Bank Sample	P value[eee]
Tumour Group				
Leukaemia	15	4 (26.7%)	11 (73.3%)	<0.001*
Lymphoma	70	44 (62.9%)	26 (37.1%)	
CNS	27	1 (3.7%)	26 (96.3%)	
Germ Cell	117	57 (48.7%)	60 (51.3%)	
Non CNS solid	50	18 (36%)	32 (64%)	
Deprivation fifth				
1	38	16 (42.1%)	22 (57.9%)	0.02*
2	52	31 (59.6%)	21 (40.4%)	
3	39	11 (28.2%)	28 (71.8%)	
4	64	31 (48.4%)	33 (51.6%)	
5	87	31 (35.6%)	56 (64.4%)	
Ethnic Group				
White	185	79 (42.7%)	106 (57.3%)	0.265
South Asian	34	11 (32.4%)	23 (67.6%)	
Other	14	8 (57.1%)	6 (42.9%)	

[eee] *denotes statistical significance

Table 6.1d Characteristics of patients who did and didn't undergo semen cryopreservation (all ages)

Characteristic	Eligible to Bank	Banked Sample	Didn't Bank Sample	P value[fff]
Tumour Group				
Leukaemia	37	12 (32.4%)	25 (67.6%)	<0.001*
Lymphoma	90	53 (58.9%)	37 (41.1%)	
CNS	46	2 (4.3%)	44 (95.7%)	
Germ Cell	125	60 (48%)	65 (52%)	
Non CNS solid	65	24 (36.9%)	41 (63.1%)	
Deprivation fifth				
1	61	29 (47.5%)	32 (52.5%)	0.01*
2	65	34 (52.3%)	31 (47.7%)	
3	51	12 (23.5%)	39 (76.5%)	
4	83	38 (45.8%)	45 (54.2%)	
5	103	38 (36.9%)	65 (63.1%)	
Ethnic Group				
White	255	101 (39.6%)	154 (60.4%)	0.776
South Asian	42	15 (35.7%)	27 (64.3%)	
Other	20	9 (45%)	11 (55%)	

The mean age at diagnosis was 22.2 years for all patients. The commonest malignant diagnoses were germ cell tumours (34.4%; 39.7% of patients who had banked semen vs 30.7% of patients who hadn't banked semen) and

[fff] *denotes statistical significance

lymphoma (24.8%; 35.1% of patients who had banked semen vs 17.5% of patients who hadn't banked semen).

In patients aged 13-17 at diagnosis, diagnoses were more evenly distributed, with leukaemias accounting for 25.6% and lymphomas and CNS tumours each accounting for 23.2% of eligible patients. However, when looking specifically at patients aged 13-17 at diagnosis who had undergone semen cryopreservation, lymphomas accounted for 32% of patients and leukaemias accounted for 28% of patients. CNS tumours accounted for only 4% of 13-17 year olds who had banked semen, but 31.6% of 13-17 year olds who hadn't banked semen.

In older patients aged 18-29 at diagnosis, 41.9% of eligible patients had a diagnosis of germ cell tumour and 25.1% had a diagnosis of lymphoma. 46% of patients in this age group who had banked semen had germ cell tumours and 35.5% had lymphomas. Amongst 18-29 year olds who hadn't banked semen, 38% had germ cell tumours and 20.6% had non-CNS solid tumours. 17 (11.3%) of those individuals who banked sperm had already fathered a child prior to undergoing fertility preservation.

83 (55.0%) of those who had banked semen prior to cancer treatment were seen again in the fertility service. 8 (9.6%) of those who were seen again in the fertility service had fathered a child since banking semen. 7 (8.4% of those who were seen again and 4.6% of those who originally banked) individuals underwent fertility treatment. In 2 cases, there was documented concomitant female factor infertility which influenced the treatment strategy used. Neither of these couples achieved a pregnancy. Of the remaining 5 individuals, all achieved a pregnancy.

78 (51.7%) of those who had banked semen prior to cancer treatment had had a post treatment sample analysed. 26 (33.3%) of those with a post treatment sample had a normal semen analysis.

114 (75.5%) of those who had stored semen were treated at LTHT. 50 (43.9%) of those treated in LTHT were under active follow up in the oncology late effects clinic.

The reasons for the differences in banking and follow-up patterns are explored in section 7.5: Discussion, Strengths and Limitations of the Fertility Preservation Work.

6.3.1 Mental Health and Fertility

It was hypothesised that having banked sperm, having a normal (fertile) post treatment semen sample and continued follow up in the haematology/oncology clinic would all be associated with decreased risk of mental ill health. Table 6.2a shows the risks of specialist mental health services contacts for individuals who had banked sperm (vs those who hadn't), those who had been seen again in fertility clinic (vs those who hadn't), those who had a fertile post-treatment sample (vs those who had a sub-fertile post treatment sample) and those who were under active oncology or haematology follow up (vs those who weren't). The risks of having mental health diagnoses recorded on inpatient HES for individuals who had banked sperm (vs those who hadn't), those who had been seen again in fertility clinic (vs those who hadn't), those who had a fertile post-treatment sample (vs those who had a sub-fertile post treatment sample) and those who were under active oncology or haematology follow up (vs those who weren't) are shown in table 6.2b The risk of any indicator of mental ill health (i.e. either a recorded contact with specialist mental health services and/or a recorded mental health diagnosis on inpatient HES) for individuals who had banked sperm (vs those who hadn't), those who had been seen again in fertility clinic (vs those who hadn't), those who had a fertile post-treatment sample (vs those who had a sub-fertile post treatment sample) and those who were under active oncology or haematology follow up (vs those who weren't) are shown in table 6.2c.

Table 6.2a Odds ratios of specialist mental health services contacts for individuals who had and hadn't banked semen, had and hadn't been followed up by fertility services, had and hadn't had a fertile post-treatment semen analysis and were or weren't under active haematology or oncology follow up[ggg]

	Number of Individuals	Odds Ratio of Specialist Mental Health Services Use	95% Confidence Intervals	
Banked Semen				
No	212	Reference		
Yes	151	0.54	0.26	1.16
Seen Again in Fertility Clinic				
Yes	83	Reference		
No	68	1.78	0.42	7.49
Normal (Fertile) Post-Treatment Semen Analysis				
No	52	Reference		
Yes	26	0.06	0.00	1.71
Under Active Haematology or Oncology Follow Up				
No	64	Reference		
Yes	50	0.76	0.10	5.68

[ggg] Adjusted for age at diagnosis, deprivation, ethnicity, stage at diagnosis, treatment type, tumour group, treatment at TYA unit, year of diagnosis

Table 6.2b Odds ratios of mental health diagnoses recorded on inpatient HES for individuals who had and hadn't banked semen, had and hadn't been followed up by fertility services, had and hadn't had a fertile post-treatment semen analysis and were or weren't under active haematology or oncology follow up[hhh]

	Number of Individuals	Odds Ratio of Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
Banked Semen				
No	212	Reference		
Yes	151	0.91	0.49	1.67
Seen Again in Fertility Clinic				
Yes	83	Reference		
No	68	0.68	0.24	1.93
Normal (Fertile) Post-Treatment Semen Analysis				
No	52	Reference		
Yes	26	0.55	0.13	2.29
Under Active Haematology or Oncology Follow Up				
No	64	Reference		
Yes	50	0.23	0.55	0.97

[hhh] Adjusted for age at diagnosis, deprivation, ethnicity, stage at diagnosis, treatment type, tumour group, treatment at TYA unit, year of diagnosis

Table 6.2c Odds ratios of specialist mental health services contact and/or mental health diagnoses recorded on inpatient HES for individuals who had and hadn't banked semen, had and hadn't been followed up by fertility services, had and hadn't had a fertile post-treatment semen analysis and were or weren't under active haematology or oncology follow up[iii]

	Number of Individuals	Odds Ratios of Mental Health Services Use and/or Mental Health Diagnosis on Inpatient HES	95% Confidence Intervals	
Banked Semen				
No	212	Reference		
Yes	151	0.82	0.47	1.42
Seen Again in Fertility Clinic				
Yes	83	Reference		
No	68	0.62	0.24	1.62
Normal (Fertile) Post-Treatment Semen Analysis				
No	52	Reference		
Yes	26	0.39	0.10	1.52
Under Active Haematology or Oncology Follow Up				
No	64	Reference		
Yes	50	0.43	0.13	1.41

There was no significant difference in risk of recorded specialist mental health for individuals who had or hadn't banked sperm, were or weren't seen

[iii] Adjusted for age at diagnosis, deprivation, ethnicity, stage at diagnosis, treatment type, tumour group, treatment at TYA unit, year of diagnosis

again in the fertility clinic, had a fertile or sub-fertile post treatment semen analysis or who were or weren't under active follow up with haematology or oncology.

With regards to recorded mental health diagnoses on inpatient HES, there was a significantly reduced risk of this amongst individuals who were still under active haematology or oncology follow up. Sperm banking or not, being seen again in the fertility clinic and results of post treatment semen analysis did not significantly impact risk of having a recorded mental health diagnosis on inpatient HES.

When both indicators of mental ill health were combined, there was no difference in risk of recorded mental ill health between those who had or hadn't banked sperm, those who were or weren't seen again in the fertility clinic, those who had a fertile or sub-fertile post-treatment semen analysis result and those who were or weren't under active haematology or oncology follow-up.

Potential reasons for the findings in this chapter are explored in section 7.5, Discussion, Strengths and Limitations of the Fertility Preservation Work.

Chapter 7 Discussion

This thesis has sought to examine the relationship between a diagnosis of cancer in childhood or young adulthood and future risk of mental ill health. Utilising a high quality population-based specialist cancer registry and data linkage methodologies, it was possible to determine the rate of specialist mental health services use amongst a cohort of long term CYP's cancer survivors.

7.1 Key findings

The key findings of this thesis were:

- CYP's cancer survivors are more likely than the general population to have received specialist mental health care, as recorded on the MHMDS or MHLDDS.
    - 10.7% of CYP's cancer survivors on the YSRCCYP had a recorded contact with specialist mental health care recorded on the MHMDS and/or MHLDDS
    - The standardised incidence ratio for specialist mental health contacts amongst CYP's cancer survivors was 173.7 (95% CI 165.6-182.1); i.e. cancer survivors are 73.7% more likely than the general population to have a recorded contact with specialist mental health care.
- CYP's cancer survivors are no more likely than the general population to have a recorded mental health diagnosis on inpatient HES
    - 12.5% of CYP's cancer survivors on the YSRCCYP had a recorded mental health diagnosis on inpatient HES
    - The standardised incidence ratio for recorded mental health diagnosis on inpatient HES amongst CYP's cancer survivors was 97 (95% CI 91-103); i.e. cancer survivors are 3% less likely than the general population to have a recorded mental health diagnosis on inpatient HES.
- Individuals diagnosed during the teenage or young adult period (aged 13 to 29 at the time of cancer diagnosis) were almost twice as likely as those diagnosed with cancer under the age of 13 to have access specialist mental health care (13-24 RR 1.92, 95% CI 1.67-2.21; 25-29 RR 1.80, 95% CI 1.54-2.11).

- Individuals treated on specialist TYA units appeared to have more recorded mental ill health than those treated on standard wards (RR 1.36, 95% CI 1.00-1.84), and this effect was more pronounced when only young people aged 18-24 were considered (RR 1.78, 95% CI 1.20-2.64).
- Individuals from more deprived backgrounds at the time of cancer diagnosis were significantly more likely to have future recorded mental ill health than those from less deprived backgrounds, with risk of recorded mental ill health increasing 5% (95% CI 3-7%) for each 1 point increase in deprivation on the Townsend deprivation index.
- Female survivors were 20% (95% CI 7-35%) more likely than males to have future recorded mental ill health.
- Stage at time of diagnosis (for non-CNS solid tumours) and white cell count at diagnosis (for leukaemias) were not associated with differing risks of future recorded mental ill health.
- Individuals with low grade CNS tumours were at increased risk of recorded mental ill health compared to those with high grade CNS tumours.
- Amongst individuals diagnosed as children (aged 0-14 at diagnosis), survivors of low grade CNS tumours were at greater risk of future mental ill health than survivors of leukaemia (RR 1.43, 95% CI 1.07-1.92). There was no significant increase in risk of future mental ill health amongst survivors of other tumour types.
- Amongst individuals diagnosed as young adults (aged 15-29 at diagnosis), survivors of low grade CNS tumours appeared to be at greater risk of future mental ill health than survivors of germ cell tumours (RR 1.23, 95% CI 0.90-1.67). There was no significant increase in risk of future mental ill health amongst survivors of other tumour types.
- Individuals treated with combined chemotherapy and radiotherapy appeared to be at lower risk of future specialist mental health services use compared to individuals treated with chemotherapy alone (RR 1.18, 95% CI 0.99-1.41).
- Individuals allocated NCSI level 3 were over twice as likely as those allocated NCSI level 2 to have recorded mental ill health (RR 2.39, 95% CI 1.74-3.25).
- Individuals diagnosed as children had an increased risk of recorded mental ill health if they were diagnosed longer ago, with those diagnosed during the period 1985-1989 appearing to be at greatest

risk (RR 2.90, 95% CI 1.95-4.33), Conversely, individuals diagnosed as young adults had an increased risk of recorded mental ill health if they were diagnosed more recently, with those diagnosed during the period 2010-2012 at greatest risk (RR 1.32, 95% CI 1.03-1.69).

- Ethnicity did not appear to significantly impact likelihood of recorded mental ill health.
- Males who had undergone semen cryopreservation appeared to be less likely to have future recorded mental ill health (RR 0.82, 95% CI 0.47-1.42) than those who hadn't undergone semen cryopreservation, although post-treatment fertility was not associated with risk of recorded mental ill health.

7.2 Clinical Implications

This thesis highlights the increased risk of contacts with specialist mental health services amongst long-term survivors of CYP's cancer. Whilst patients who are under active follow-up often have the opportunity to complete holistic needs assessments[369], which may identify potential mental health difficulties as they evolve, many long-term survivors will have been discharged from specialist follow-up, and others will be seen only infrequently[99].

Clinicians providing long-term follow-up or survivorship services, may feel less confident assessing and discussing mental health problems than they are in, for example, talking about risks of cardiac failure or secondary malignancy. It is therefore essential that clinicians in these roles have adequate training on both the assessment and recognition of mental health disorders, as well as the mental health support and treatment available locally, and the best ways for patients to access these services. In particular, clinicians should be aware of the increased risk of mental ill health amongst at risk groups, including those diagnosed with cancer as teenagers and young adults, females and those from deprived backgrounds.

Currently, long-term follow-up care is determined largely by risk of physical late effects[99]. Whilst CYP's cancer survivors with physical health problems are at increased risk of mental ill health[157], not all individuals who may develop mental health problems will currently be routinely followed up in specialist care. Particular attention should be drawn to survivors of low-

grade CNS tumours, and individuals treated with neither chemo- nor radiotherapy, who appear to be at considerable risk of mental ill health but who may not be monitored closely in long-term follow-up services.

Low grade CNS tumours are associated with increased risk of future mental ill health. These tumours are common[27] and, due to their generally good prognosis[370], survivors of them account for a considerable proportion of the entire CYP's cancer survivor population (27% of the cohort in this study had a low-grade CNS tumour). However, individuals with low-grade CNS tumours, may be treated with only surgery[370], or even simple monitoring[371]. These individuals are thus at low risk of physical late effects and therefore likely to be discharged from specialist services[99]. This highlights the discrepancy between risk of physical late effects and risk of mental health sequalae. It may, therefore, be beneficial in future to ensure that survivors of CYP's cancer are educated on potential mental health difficulties, and how and where to access support should these issues arise. Additionally, it may be that future risk-stratification systems take into account risk of mental health problems when deciding whether or not to discharge a patient from specialist cancer care. Treatment summaries should be sent to all primary care clinicians, and should clearly highlight risks of mental ill health which could be seen in cancer survivors, particularly amongst those who are no longer being followed up in specialist cancer services.

Risk of future mental ill health is higher amongst female CYP's cancer survivors. Although cancer is more common in boys than in girls, incidence is increasing more rapidly in girls, thus potentially narrowing this gap[14]. Amongst TYA, cancer is more common in females than males[15]. The increasing incidence of cancer in young girls may lead in future to a greater number of mental health problems in this cohort.

7.3 Discussion, Strengths and Limitations of the Study Cohort

The study cohort were selected from the YSRCCYP. The methods used to link MH episodes to the YSRCCYP are described in detail in section 3.1: The Yorkshire Specialist Register of Cancer in Children and Young People.

The cohort are described and compared with the Yorkshire population in Chapter 4: Cohort Description.

7.3.1 The Yorkshire Specialist Register of Cancer in Children and Young People Cohort

A major strength of this cohort was that they were population-based, rather than opt-in, meaning that all individuals on the YSRCCYP who had survived over 5 years were included and not just a self-selecting group who had returned questionnaires or agreed to further follow up. This compares to other, large cohorts which have explored the long-term mental health of cancer survivors[108,161,262,267]. Population-based registers have the advantage of including all individuals who have had a cancer diagnosis and avoid potential issues with non-response bias, which may occur with questionnaire-based or opt-in cohorts.

Additionally, the YSRCCYP includes data on TYA diagnosed under the age of 30, whilst other cohorts only look at children, excluding those young people diagnosed over the age of 15[267] or 21 years[108]. Historically, TYA have been excluded from the majority of studies into cancer[314]. The systematic review aspect of this work found only 5 of 67 studies focussing on TYA. It is therefore an important strength of this study that this group have been included.

A further strength of the YSRCCYP is that treatment data is included for all individuals, so it is possible to look at the long-term impact of specific chemotherapy and radiotherapy treatment as well as surgical interventions.

An initial analysis of the cohort looked at the assignment of NCSI levels which are described in Chapter 4: Cohort Description. It was observed that NCSI levels were more likely to be assigned to patients who were younger at the time of diagnosis. This may be down to differences in referral rates to long term follow up services between paediatric and adult oncologists. It may also reflect the fact that a higher percentage of older patients are treated outside of LTHT and are thus not being seen within the LTHT follow-up services.

The use of Onomap software to impute absent ethnicities to the YSRCCYP meant that ethnicity data in this cohort was almost complete, and allowed

ethnic group to be explored as a potentially important factor. Data on deprivation status and diagnosis were also complete, which enhanced the quality of analyses looking at these factors.

Cancer diagnoses were classified according to the ICCC and Birch classification systems, which are described in full in section 1.1.3: Cancer Classification. Although these are robust, validated systems[25,26], alternative classification systems exist and have slight differences. As well as the advantages associated with being well established and validated systems, there are also benefits when comparing work with internationally published results, which is much simpler and easier if the same classification systems are used. The Barr Classification Scheme for Adolescent and Young Adult Cancer is another system which is sometimes used, although this is very similar to the Birch system. The major categories most used by epidemiological studies are the same, and thus comparisons between studies using the Birch and Barr systems are possible and likely to be valid[372].However, there are also drawbacks. Some groups are extremely heterogeneous, for example CNS tumours, and it is consequently difficult to draw conclusions about such a varied population. For the purposes of this thesis, the distinction was made between high- and low-grade tumours, but this is not always the case. Conversely, groups such as retinoblastoma account for such small numbers of individuals that it is very difficult to reliably analyse them in detail without major international collaboration.

7.3.2 Population Data

Similarities and differences between the YSRCCYP and also described in Chapter 4: Cohort Description. The YSRCCYP cohort had a similar ethnic make-up to the Yorkshire population as a whole, and patterns of deprivation were also similar. However, the YSRCCYP had many more males (59.8% of YSRCCYP cohort compared to 49.2% of the whole Yorkshire population). This likely reflects the fact that cancer diagnoses in childhood are more common in males[14]. Although cancer diagnoses in the TYA age group are more common in females[15], the YSRCCYP collected data on childhood cancer (diagnosed under the age of 15 years) for 16 years before data on older CYP (aged 15-29 at diagnosis) was collected, which likely explains the

gender difference. The similarities between the ethnic and deprivation mixes seen in the YSRCCYP cohort and the whole Yorkshire population are a strength of this work. However, gender differences between the YSRCCYP cohort and the Yorkshire population may limit the generalisability of this work, although the calculations used to look at differences in rates of recorded mental ill health did take into account the gender mix of the populations.

The data provided on the Yorkshire population was limited to an aggregated table of data, rather than individual-level data. This was due to difficulties obtaining data from NHS Digital, and concerns regarding potential identifiability of individuals. Despite multiple conversations with the data provider, it was not possible to obtain more granular data. Data was provided broken down by gender and age-bracket only. This limits the work, as it was impossible to adjust for factors such as deprivation status and ethnicity, which potentially could have impacted the results obtained. Socioeconomic status is causatively associated with childhood cancer risk, albeit as a probable proxy marker for factors such as parental smoking[373], as are gender[28] and ethnicity[374], and it would therefore have been important to adjust for socioeconomic status and ethnicity if possible. A further limitation to data being provided in this format was that it wasn't possible to know whether individuals had had multiple mental health service contacts or recorded mental health diagnoses on inpatient HES in different years. Whilst it was possible to look at the number of individuals with a mental health services contact or recorded mental health diagnosis on inpatient HES for each year, it wasn't possible to work out what proportion of the population had any contact over the time period for which data were available. It is possible that there are differences in the way mental health services are accessed between the YSRCCYP cohort and the rest of the population, for example in one group there may have been lots of contacts made by individuals who were seen only once or twice whilst in the other there may have been a similar number of contacts but made by a smaller number of individuals who had multiple interactions with mental health care. The lack of individual-level population data means that this could not be explored in this thesis. Equally, it is possible that a similar number of individuals had

contacts but that individuals in one group had far more contacts than in the other, and again this could not be explored without having individual-level population data.

Yorkshire is a large area, with a population of 5.3 million[349]. It does have some differences compared to the overall population of the United Kingdom. Yorkshire has a slightly larger white population than the U.K. as a whole, with 88% compared to 86% of the population identifying as white. Individuals of South Asian ethnicity make up 5.3% of the population of the U.K., compared to 6.0% of the Yorkshire population. There are also areas of the U.K. with much higher proportions of Black and East Asian individuals than are seen within Yorkshire[349]. These differences probably don't markedly limit the applicability of the data to the U.K. as a whole, but may mean it isn't applicable to specific smaller regions with a very different ethnic make-up. Yorkshire is also more deprived than the rest of the U.K., with around a quarter of the population living in areas within the most deprived quintile[375], whilst in the U.K. as a whole the population are equally distributed throughout the quintiles. This difference in deprivation may also limit the applicability of the results of this work to the rest of the UK.

7.4 Discussion, Strength and Limitations of the Mental Health Work

The work exploring the risk of mental ill health amongst survivors of childhood and young adult cancers demonstrated an increased risk of specialist mental health services use in this cohort. This is in keeping with work from other centres, which have suggested increased mental ill health amongst survivors of CYP's cancers[161,267], including a previous Canadian population-based study[322]. Survivors of CYP cancer were no more likely than population controls to have recorded mental health diagnoses on inpatient HES. This may reflect that fact that co-morbidities are not always well recorded on such datasets, and that if the mental health diagnosis if not the primary reason for admission, this may well not be recorded[376]. This limitation is explored further in section 7.5.1 Mental Health Data Sets. It is suspected that this lack of difference represents poor recording for both

cancer survivors and controls, and it is not possible to make any statement about risk of mental illness as a result.

The reasons for increased mental health services use are likely to be multifactorial. The increased prevalence of physical health problems which would be expected in this cohort may well be a contributory factor, as the link between physical and mental health is well documented[210,211]. The emotional impact of a cancer diagnosis is again well recognised, and at least some of the increased mental health problems seen may directly result from this, with PTSD being a direct result of the cancer diagnosis for some individuals[294,321]. Equally, some issues may result from treatment itself having direct effects on the brain and impacting on future mental health, particularly cranial radiotherapy or intrathecal chemotherapy[256], or from the tumour itself in the case of CNS tumours.

Individuals diagnosed during the TYA period were at greater risk of future mental health difficulties than those diagnosed as children. This finding was in keeping with literature which has suggested an increased risk of mental ill health in those diagnosed with cancer during the TYA age group[240,265,322]. This is likely to be explained by the already-known association between physical ill health during adolescence and mental ill health[210–212], and the

the considerable burden of adjusting to a life-changing illness in adolescence[215], with similar patterns seen in other serious illnesses affecting young people[377]. The increased risk of mental health contacts seen in those treated on specialist TYA units, however, was unexpected. Young adults treated on specialist TYA units are more satisfied with many aspects of their care, including having company of a similar age, provision of space to study, and leisure facilities[378], and it was anticipated that these factors would have led to a reduction in risk of long-term mental ill health. Additionally, those young people treated in adult facilities report negative experiences relating to isolation, lack of empathy from staff, and inappropriate treatment environment[379], which could be expected to contribute to greater risk of future mental health problems. However, there may be some downsides to being treated in an apparently age-appropriate unit. Relationships may be forged with fellow young people, some of whom will not survive their illness,

which could lead to both natural grief reactions, and survivors' guilt[380]. Forging close friendships with other cancer patients may also lead to jealously from existing friends and neglect of those relationships, leading to difficulty reintegrating into previous social circles after treatment. Young people treated on specialist TYA units also receive considerable support from specialist nurses and youth support workers, which often continues long after treatment finishes[381]. These specialist workers may be able to help young people navigate the healthcare system, encouraging them to seek medical advice for any difficulties, communicating with general practitioners and other professionals about any concerns, and assisting in obtaining onward referrals where these are appropriate. It is unclear, therefore, whether the increased risk of specialist mental health services use represents a true increase in disease prevalence, or whether these individuals have better healthcare support and are therefore better at accessing specialist services when they are required.

The increased risk of mental ill health amongst individuals from more deprived backgrounds also reflects risk factors seen in the general population, with greater mental health problems seen among individuals from more deprived backgrounds generally[382,383].

Females in the general population are at higher risk of mental health difficulties than males[384], and this pattern was reflected in CYP's cancer survivors. There is some evidence that females appear more susceptible to earlier stressors than males, which may partially explain this result[385,386].

It was unexpected that there was no increased risk of mental ill health seen in those with higher stage disease at presentation. This may be a result of smaller numbers of survivors of more advanced disease meaning that a difference is not detected, or it may be that individuals with more advanced disease are given more intensive support which ameliorates some of the impact of their disease and treatment.

The increased risk of mental ill health seen in survivors of low-grade CNS tumours was also unexpected, as it was hypothesised that survivors of high-grade CNS tumours would have worse mental health as a result of intensive treatment and residual disability. These survivors made up a notable

proportion of the study cohort, and so it is unlikely to be due to small numbers. It may, however, be a result of reduced support offered to individuals who are perceived to have had less intensive treatments.

The decreased risk of mental ill health seen in individuals treated with combined chemo- and radiotherapy was also surprising, but may explain why individuals with more advanced disease didn't have the increase in mental ill health which had been initially expected, and may also explain why survivors of low-grade, rather than high-grade, CNS tumours, had increased risk of mental ill health.

It was, however, counter-intuitive that those allocated NCSI level 3 had higher risk of specialist mental health services use, as these are likely to be some of the same individuals who received both chemo- and radiotherapy. However, because NCSI levels were not available for all individuals, smaller sample sizes may have impacted on the reliability of these results. Additionally, like those treated on specialist TYA units, those allocated NCSI level 3 were likely to be receiving more healthcare support and thus it may be that they were better at accessing the specialist care they required, rather than having a genuinely increased disease prevalence.

The effects of time period of diagnosis were also somewhat unexpected, as it was anticipated that individuals diagnosed longer ago would be at greatest risk of mental ill health regardless of age at diagnosis, due to the more intensive treatments used longer ago. However, as previously stated, treatment intensity may not correlate well with mental health risk. Additionally, in those diagnosed as teenagers, it may be that their mental health difficulties emerged more quickly and thus were seen before they reached the 5 year period where they were classed as long-term survivors.

7.4.1 Mental Health Data Sets

The MHMDS and MHLDDS have the major strength that they are recording use of specialist mental health services, and thus all individuals with a recorded contact on these data sets will have been assessed as having a mental health condition requiring specialist care by a healthcare professional. This is an advantage over much work in this field which relies on self-reported mental health difficulties[172,259,262,280,282,290] or implies

diagnoses from prescribing data[156,258,265]. The converse of this is that these data sets only record specialist mental health care, and not individuals who are treated in primary care, or those with mental health problems who are either undiagnosed or who are not undergoing active treatment.

Data from the MHMDS and MHLDDS were only available for a relatively short time period, from 2006 to 2016, meaning that mental health services use out with this period would not have been captured in the analysis in this thesis.

A potentially important limitation of the MHMDS and MHLDDS is that they depend on accurate data being recorded and coded. Although the quality of coding on HES records in general has improved noticeably in recent years, there is always the possibility that a diagnosis or admission has been recorded inaccurately[330]. Additionally, linkage errors may mean that records are not identified accurately. Work looking at Paediatric Intensive Care admissions has shown a low false match rate of 0.2%, but quite a high missed match rate of 4.1%[387]; if similar rates occurred when the YSRCCYP was linked to the MHMDS and MHLDDS then the true prevalence of mental health services use amongst CYP's cancer survivors would have been underestimated.

Another major limitation of the data sets used was that, for the time periods where we were able to obtain data, use of mental health care services specifically for children and adolescents were not included. These services have been included in HES mental health data sets more recently and future analyses of these data sets which do include young people's mental health services would be a useful addition to this work. Children diagnosed with cancer very early in life may develop mental health problems many years after their treatment finishes, but still be classed as "children" at this time and thus be treated within children's services. It is therefore an important limitation that the datasets provided did not include the services who would have provided care for these young people.

The exploration of recorded mental health diagnoses on the inpatient HES database made some attempt to identify individuals who have a mental health diagnosis but who were not necessarily in receipt of specialist mental

healthcare. However, these are limited by only being available for individuals who had at least one inpatient hospital stay during the period for which data were available. Although the high rate of physical health problems amongst CYP's cancer survivors[111,184,275] means that many will have had at least one admission, there will still have been a considerable number who were never an inpatient. There have also been concerns that recording of co-morbidity lacks accuracy and has a particularly poor negative predictive value, meaning that the absence of a recorded co-morbidity does not mean that it is not present[376]. Inpatient HES data, however, was available for a longer period (1998-2017) than the mental health specific data sets. The inclusion of these records will have captured individuals who had an inpatient stay for a mental health issue between 1998 and 2006 and from 2016 to 2017, who would not have been included in the mental health data sets. However, looking solely at inpatient mental health stays would not have captured all specialist mental health services use in these time periods. The availability of this data over a longer time period may explain why a greater percentage of survivors had a mental health record on inpatient HES than on the MHMDS and/or MHLDDS (12.5% vs 10.7%). Additionally, the fact that this dataset may have captured some mental health issues which may not have been severe enough to warrant specialist care could also explain the increased number of contacts.

Overall, at the present time, the specific mental health datasets (MHMDS and MHLDDS) are likely to be considerably more useful when assessing mental illness rates than the inpatient HES database.

An additional potential limitation is the fact that a small number of individuals will opt out of their data being recorded and shared by NHSDigital, through the National Data Opt-Out Programme[388]. As of 2019, 2.74% of the population had opted out of having their data shared in this way[388]. Data from these individuals will not appear on any extracts from NHSDigital. This should not be a big limitation, as it would be assumed that roughly equal proportions of the registry population and whole Yorkshire population would have opted out. Additionally, the highest rates of opt-out are in the over

60s[388], who would not have been included in the work done as part of this thesis.

7.4.2 Primary Care Data

A notable limitation to this work is the absence of data from primary care. It is known that the majority of mental health care is provided in general practice[163], and one of the main conclusions of the systematic review of the literature was that inclusion of data regarding primary care access for mental health problems would be beneficial. Although there are considerable difficulties identifying mental health problems from primary care records due to issues with coding[389], this research would have been considerably strengthened if primary care data could have been included, despite its presumed limitations.

7.4.2.1 Reasons for Lack of Primary Care Data

At the start of the study period for this Doctor of Philosophy, it was hoped that data would be available from primary care. Unfortunately, despite work to request these data and gain ethical approval to use it beginning in early 2017, data wasn't received by the University of Leeds until late 2019. There were then further delays as University systems did not sufficiently meet data security levels to allow the data to be accessed. Data were only available in an accessible format in November 2019, however with the period of study for this Doctor of Philosophy ending in January 2020, it was not considered feasible to analyse these data for inclusion in this thesis.

7.5 Discussion, Strengths and Limitations of the Fertility Preservation Work

Considerably fewer patients aged 13-17 at diagnosis had banked semen compared to those aged 18 and over. This is likely to reflect the fact that many younger patients have not reached sexual maturity and are unable to produce a sample with sufficient spermatozoa to bank; in a large multinational study of adolescents undergoing fertility preservation, likelihood of producing an azoospermic sample was inversely correlated with age[390]. Patients under 18 are also likely to be accompanied to their appointment by a parent or guardian, and there is evidence that the presence of an

accompanying adult reduces the likelihood of producing a sample, probably as a result of embarrassment around masturbation[391].

The semen banking rate amongst individuals with CNS tumours was very low compared to all other tumour groups. This may be due to the fact that many CNS tumours are not treated with gonadotoxic therapies and thus there would be no indication to refer for fertility preservation.

There was a notably lower rate of semen banking amongst those in the middle deprivation fifth. This is an unusual finding for which there is no obvious explanation, and this may be a result of the small numbers in this study.

As suggested by a previous study, it is likely that fertility preservation is associated with decreased mental distress regarding sub-fertility[368] and this may explain why fewer men who had stored semen had recorded mental ill health. Although a significant difference was not seen for recorded contact with specialist mental health services between those who had and hadn't banked semen, there was a suggestion of reduced risk in those who had stored semen (OR 0.54, 95% CI 0.26-1.16).

It was also anticipated that having a normal semen analysis following treatment would also lead to a reduction in incidence of mental ill health requiring specialist treatment, and this was not seen in this study. This may reflect the relatively small number of patients for whom we had post-treatment data rather than a genuine lack of effect. Indeed, one of the major limitations to this chapter was the small number of individuals for whom data were available, and it is difficult to draw any robust conclusions based on such small numbers. The large confidence intervals are almost certainly a result of such small numbers, and it may be that a larger study would find results which achieved statistical significance.

A relatively low number of our cohort had banked sperm compared to other reports. Even studies looking solely at younger patients reported banking rates from 43.8% to 83%[392,393]. However, the higher rate was seen in a study recruiting patients who had already been referred to fertility services and it is unclear how many of the overall number of patients diagnosed with cancer would have been included. It is also worth noting that rates of semen

cryopreservation have been increasing year on year[393], and an older paper reported lower rates of 28.1%, which are much lower than the rate we found[394]. A paper reporting solely on lymphoma patients, who made up a large proportion of our cohort, reported lower rates of 40%, which is comparable to our findings[395].

Data were not available on how many of our cohort were referred for fertility preservation but were either unable to produce a sample or produced an azoospermic sample unsuitable for freezing. Patients with testicular tumours and Hodgkin's lymphoma, who account for a notable number of our cohort, have previously been shown to produce poorer quality semen[396] and it may be that a number of samples which were unsuitable for freezing accounted in some part for the low overall banking numbers in this cohort. Additionally, a number of the younger patients in our cohort may not have completed puberty and may not have been sexually mature enough to actually produce a suitable sample[397].

Despite the small number of patients banking sperm being an obvious limitation of this work, a major strength is that over 50% of patients who did bank semen had had a post-treatment semen sample analysed. This compares of rates of 40-42% in other studies[395,396].

Despite the relatively small nature of this study, we have shown that having undergone fertility preservation is associated with decreased risk of mental ill health requiring specialist care in long-term cancer survivors. This is further evidence to support the routine referral of young men with cancer to fertility services prior to undergoing cancer treatment where it is safe to do so.

7.6 Future Work

7.6.1 Recommendations for the Yorkshire Specialist Register of Cancer in Children and Young People

The YSRCCYP has been an invaluable data source throughout this work. Nonetheless, future work could be enhanced by the inclusion of additional data.

A reliable indicator of whether or not an individual has undergone HSCT, whether this was an autograft or an allograft, and details on the donor

(match status, related or unrelated) would be extremely valuable. The intensity of treatment for HSCT may pre-dispose individuals undergoing it to multiple future problems, which may include mental health and fertility issues, and being able to readily identify them so that they can be studied as a separate group would be potentially very useful. The number of individuals treated with HSCT has been reported in other cohort studies[108,267,292], and thus there is a need for this information to be collected.

More reliable, detailed data on the treatment received by individuals, including cumulative dose of high-risk drugs such as anthracyclines and total radiotherapy doses, would be helpful and would allow more detailed exploration of the links between treatment and future outcomes. At the present time, another PhD student is looking at using data linkage between the YSRCCYP and electronic hospital records to provide this data, so it may be that in future, this data is much more readily available.

It would also be useful to be able to explore whether being under regular specialist oncology or haematology follow-up impacted future risk of mental ill health. Therefore, a reliable marker of when an individual was last reviewed by specialist services would be a helpful thing for the YSRCCYP to include.

In addition to data on follow-up, if it were possible to access data on physical health and late effects, this would allow testing of the hypothesis that at least some of the increased mental ill health seen in cancer survivors was related to increased physical health difficulties. Although it may be difficult from a practical point of view, if the registry were able to maintain a list of ongoing late effects, this would allow more exploration of the link between physical and mental ill health. This is likely to be a difficult thing to do in practice due to data regulation laws not allowing the registry to keep linked data from HES, which has previously been used to explore cardiovascular and respiratory health problems[111,398], in the registry itself.

7.6.2 Mental Health

As previously described, the inclusion of primary care data would have greatly enhanced this thesis. Work exploring mental health diagnoses, prescriptions of drugs for mental health disorders and referrals to specialist

services would be extremely valuable and has the potential to form the basis of a future thesis.

Future analysis of the newer mental health data set (the MHSDS), which includes data on use of services specifically for children and adolescents (i.e. the Child and Adolescent Mental Health Service, or CAMHS), would be valuable and would be of particular interest when looking at the long-term mental health of those diagnosed with cancer at a very young age. It is important that these young people are not overlooked in future analyses. Given the relationship between mental health difficulties early in life and future mental health outcomes[189,190,204], it is important that use of CAMHS services amongst cancer survivors can to be fully explored.

More granular data on the mental health of the Yorkshire population, including individualised data to allow for adjustment for socioeconomic status as well as age and sex would also enhance any future work. This would also allow comparisons between the ways mental health services are accessed so that number of contacts per individual could be explored, allowing more in-depth analysis of the potential differences between the ways in which cancer survivors and the wider population access specialist mental health care.

7.6.3 Fertility

The work looking at the impact of fertility preservation on mental health services use suggested a decreased risk of mental ill health in individuals who had undergone semen cryopreservation. Further work should focus on attempting to replicate this study on a larger scale.

Prospective cohort studies which also record data on referrals to fertility services and patients who either decline to produce semen or are unable to produce a sample suitable for cryopreservation would be an important next step. It would be useful to record both the demographic and disease characteristics of these individuals. Analysis should focus not only on the differences between those who did and did not undergo fertility preservation, but on potential differences between those who chose not to bank semen and those who would have chosen to but who were unable to.

Additionally, future work should include analysis of the impact of fertility preservation work in females, including both oocyte and ovarian tissue storage.

7.7 Conclusion

This thesis has illustrated the increased risk of specialist mental health services use amongst survivors of childhood and young adult cancers compared to the wider population in Yorkshire. Groups at particular risk of mental ill health have also been highlighted, and include females, those diagnosed as teenagers and young adults, those from more deprived backgrounds, survivors of low-grade CNS tumours, and those treated without chemo- or radiotherapy. Future work should explore the reasons behind these associations, and should include the analysis of primary-care and CAMHS services, as well as more detailed data on treatment received.

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Appendix A: List of Fields Recorded in the Yorkshire Specialist Registry of Cancer in Children and Young People

This appendix lists all available fields from the YSRCCYP, which is described in Chapter 3: Methods and Data Sources.

- General details
  - Patient ID
  - NHS number
  - Date of birth
  - Date of death
  - Forename
  - Surname
  - Twin
  - Record complete
  - Reason not complete
  - Sex
  - Ethnicity
  - Source details
  - Seen at Leeds Paediatric Oncology department?
  - Seen/tretated at TCT ward?
  - MDT meeting type
  - Comments (free text)
  - Register status
  - Reason not registered (if applicable)
- Diagnosis
  - Pathology number
  - Date of diagnosis
  - Morphology
  - Topography
  - Staging
  - Laterality
  - Basis
  - White blood cell count
  - Height (cm) at diagnosis
  - Weight (kg) at diagnosis
  - Diagnosis status
- Address
  - Address
  - Postcode
  - Verified address?
  - Time at address
- Surgery details
  - Date of surgery
  - Did patient refuse surgery?
  - OPCS code
  - Outcome code

- Radiotherapy details
    - Date of radiotherapy
    - Did patient refuse radiotherapy?
    - Has patient had RIAT?
    - Has patient had TBI?
    - Is the treatment curative?
    - Is the treatment completed?
    - Site
    - Total dose
    - Gray
    - Fractions
- Chemotherapy details
    - Date of chemo
    - Did patient refuse chemo?
    - Is the treatment completed?
    - Is there a clinical trial?
    - Which trial?
    - Trial arm
    - Regimen
    - Drug names
- Relapse details
    - Date of relapse
    - Topography
- Hospital details
    - Hospital type (treating/referring/other)
    - Hospital address
    - Consultant
    - Unit number
- Follow up details
    - Date of follow up
    - Imputed?
    - Comments (free text)
    - No treatment?
    - Reason for no treatment
    - Hospital
    - GP/Consultant
- Follow up status
    - Last known status

Appendix B: List of Fields Available from the Mental Health Minimum Dataset and Mental Health and Learning Disabilities Dataset

This appendix lists all provided fields from the MHMDS and MHLDDS, which are described in Chapter 3: Methods and Data Sources.

Mental Health Minimum Dataset

- Dataset ID
- Unique Record ID
- Provider Organisation Code
- Commissioner Code
- Reporting Period
- Start Date of Reporting Period
- End Date of Reporting Period
- Electoral ward of usual address
- Primary Care Trust of Residence
- Gender
- Marital Status
- Primary Care Trust of GP Practice
- Ethnicity
- Year of First Known Psychiatric Contact
- Care Spell Identifier
- Spell Identifier
- Number of Spells in Reporting Period
- Specialty Function Code
- Episode Start Date
- Source of Referral
- Episode End Date
- Spell End Code
- Spell Days Within Reporting Period
- Suspended Days in Reporting Period
- Suspension Reason
- Care Programme Approach Standard Days
- Care Programme Approach Enhanced Days
- Care Programme Level
- Occupation of Care Co-ordinator

- Date Care Programme Approach Care Co-Ordinator Last Seen
- Marker of Mental Health Care Without Patient Consent
- Number of Social Services Statutory Assessments for Community Care
- HONOS assessment First Score
- Date of First HONOS Assessment
- HONOS assessment Most Recent Score
- Date of Most Recent HONOS Assessment
- Worst Ever HONOS Assessment Score
- Date of Worst Ever Score on HONOS Assessment
- Best HONOS Assessment Score in Last 12 Months
- Date of Best Score in Last 12 Months on HONOS Assessment
- Mental Health Bed Days
- Mental Health Medium Security Bed Days
- Intensive Mental Health Care Days
- Acute Home Based Mental Health Care Days
- NHS Community Care Bed Days
- Indicator of Stay in non-NHS Residential Community Care
- Day Care Attendances (NHS Sites)
- Day Care Attendances (non-NHS Sites)
- Indicator of Attendance at Sheltered Work Facility
- Out-Patient Consultant Attendance
- Community Psychiatry Contact
- Clinical Psychology Contact
- Occupational Therapy Contact
- Marker of Mental Health Social Worker Involvement
- Home Help Visit
- Electroconvulsive Therapy Treatments
- Number of Admissions
- Number of Discharges
- Type of Service/Team Patient Referred To
- Physiotherapy Contact
- Consultant Psychotherapy Contact
- Social Worker Contact
- Outpatient Did Not Attend
- Day Care Did Not Attend
- Contacts with NHS Direct for Mental Health
- Care Programme Approach Review
- Method of Ascertaining Spell Start and End Date

- Postcode District
- Age at Start of Mental Health Care Spell
- Age at End of Mental Health Care Spell
- Age at Start of Reporting Period
- Age at End of Reporting Period
- Age at Date of First Inpatient Review
- Age at Date of Last Review in Reporting Period
- Age at Date Last Seen by Care Programme Approach Team
- Age at Date of Detention under Mental Health Act
- Age at Date of First Electroconvulsive Therapy Treatment
- Age at Date of Admission
- Age at Date of Discharge
- Age at Date of First HONOS Assessment
- Age at Most Recent HONOS Assessment
- Number of Concurrent Legal Statuses
- Number of Concurrent Mental Statuses
- Care Spell Number in Reporting Period
- Calculated Out-Patient Attendances
- Calculated Out-Patient Did Not Attends
- Calculated Day Care Attendances
- Calculated Day Care Did Not Attends
- First, Most Recent ICD Diagnosis
- Employment Status
- Weekly Hours Worked
- Settled Accommodation Indicator
- Accommodation Status
- Valid NHS Number Flag
- Valid Postcode Flag
- LSOA

Mental Health and Learning Disabilities Dataset

- Electoral ward of usual address
- Gender
- Marital status
- GP Practise Code
- Ethnicity
- Year of First Known Psychiatric Care
- Episode Start Date
- Episode End Date
- Postcode District
- Reason for End of Healthcare Spell
- Spell ID
- Person ID
- Provider Organisation Code
- Valid NHS Number Flag
- Valid Postcode Flag
- LSOA
- County
- Local Authority District/Unitary Authority
- Age
- Date of first noticeable change in behaviour or mental state
- Date of first positive psychotic symptom
- Date at which positive psychotic symptom has lasted for one week
- Emergent Psychosis Date
- Psychosis Treatment Start Date
- Crisis Plan Creation Date
- Crisis Plan Last Update Date
- Ethnic Code Category (Cleansed)
- Total Number of Days Between Start and End of Ward Stay
- Total Number of Days Between Start and End of Ward Stay (Cleansed)
- Total Number of Days Between Start and End of Ward Stay, Minus Home Leave
- Organisation Code (Residence Responsibility)
- Organisation Code (GP Practice Responsibility)
- Clinical Commissioning Group of GP
- Indicator of Open Care Programme Approach Episode at End of Reporting Period

- Indicator of Open MHA Episode at End of Reporting Period
- Indicator of Open SCT Episode at End of Reporting Period
- Indicator of Open Recall Episode at End of Reporting Period, where Recall Has Not Expired
- Indicator of Open Spell at End of Reporting Period, with Valid Recorded Primary Diagnosis within the Previous 12 Months
- Employment Status of Most Recent Event
- Settled Accommodation Status of Most Recent Event
- Settled Accommodation Indicator for Most Recent Event
- Indicator of Open Spell at End of Reporting Period and Care Programme Approach Review within the Previous 12 Months
- Indicator of Open EIT Team Episode at End of Reporting Period
- Indicator of Open AOT Team Episode at End of Reporting Period
- Indicator of Open WRDST or PROSP Episode at End of Reporting Period
- Length of Spell (in Days)
- Cluster Code for Most Recent Open Cluster Episode
- Indicator of Open Care Approach Episode for More Than 365 Days
- Number of Mental Health Act Admissions
- Total Number of Discharges in the Reporting Period
- Total Number of Healthcare Provider Contacts in the Reporting Period
- Number of Attended Healthcare Provider Contacts in the Reporting Period
- Number of Days Between The Start and End of a Delayed Discharge Episode
- Number of Distinct Mental Health Commissioner Codes
- Total Number of Day Attendance Contacts
- Number of Attended Day Attendance Contacts
- Indicator of AWOL Episode
- Legal Status Classification Code (Cleansed)
- Most Restrictive Legal Classification During Episode
- Month ID the Record was Given
- Financial Year of Episode
- Marker of Inactive Episode
- Marker of Open Ward Spell at the End of a Period of Learning Disability Care, Plus Intensity of Care
- Marker of Open Episode with Learning Disability Team
- Marker of Open Episode with Learning Disability Specialty

- Marker of Open Episode with Learning Disability Treatment Function
- Marker That Patient is Limited by Memory or Concentration, and that Symptoms Began Before the Age of 18 years
- Indicator That HONOS Assessment was Carried Out in Past 12 Months
- Indicator That Patient Had a Learning Disability at the Start of the Reporting Period
- Indicator of Open Episode with Learning Disability Services
- Indicator That Patient Had a Mental Health Issue at the Start of the Reporting Period
- Indicator of Open Episode with Mental Health Services
- Trace Status of NHS Number
- Organisation Code of Organisation that Assigned Local Patient Identifier
- Date Smoking Status Recorded
- Date Disability Questionnaire Completed
- Smoking Status
- Answer to Disability Question
- Answer to Behavioural and Emotional Question
- Answer to Hearing Question
- Answer to Manual Dexterity Question
- Answer to Memory or Ability to Learn Concentrate or Understand Question (if Under 18 at Symptom Onset)
- Answer to Memory or Ability to Learn Concentrate or Understand Question (if 18 or Over at Symptom Onset)
- Answer to Mobility and Gross Motor Question
- Answer to Perception of Physical Danger Question
- Answer to Personal, Self-Care and Continence Question
- Answer to Progressive Conditions and Physical Health Question
- Answer to Sight Question
- Answer to Speech Question
- Answer to Autism Spectrum Conditions Question
- Answer to Other Question

Appendix C: Directed acyclic Graphs

This appendix shows DAGs with each possible exposure highlighted as the primary exposure.

Figure C1: A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and “deprivation” highlighted as the primary risk factor of interest (exposure), together with all other variables.

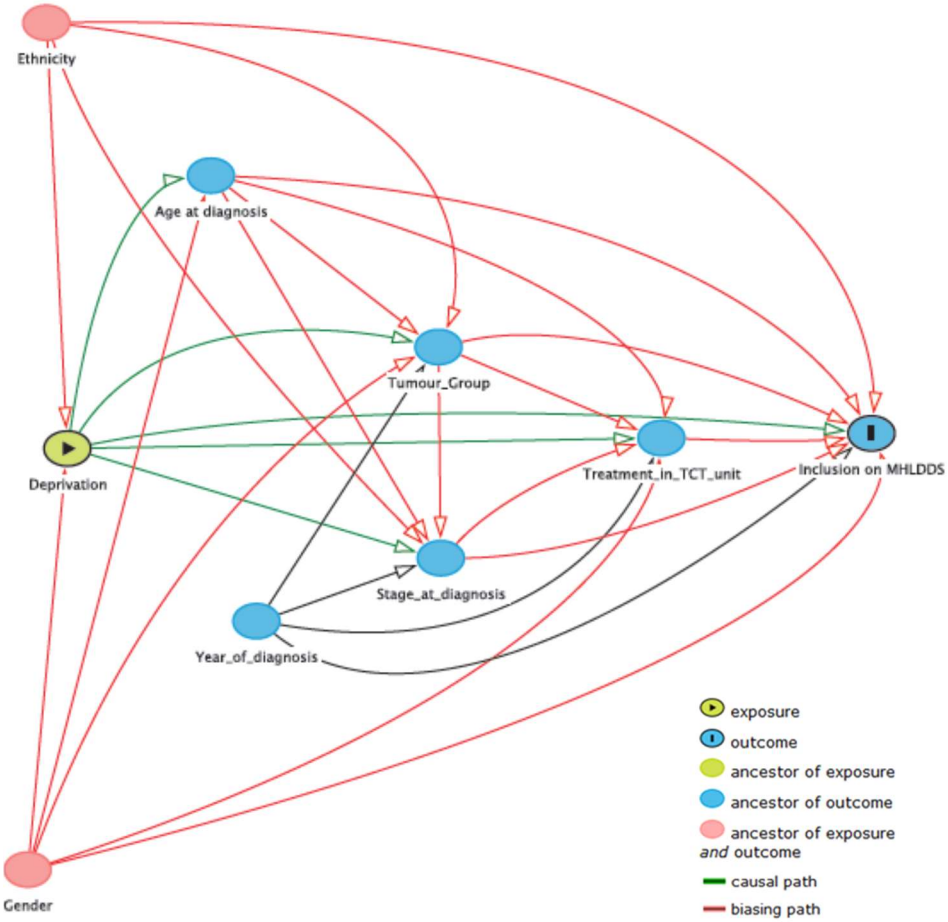


Figure C2: A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and “ethnicity” highlighted as the primary risk factor of interest (exposure), together with all other variables.

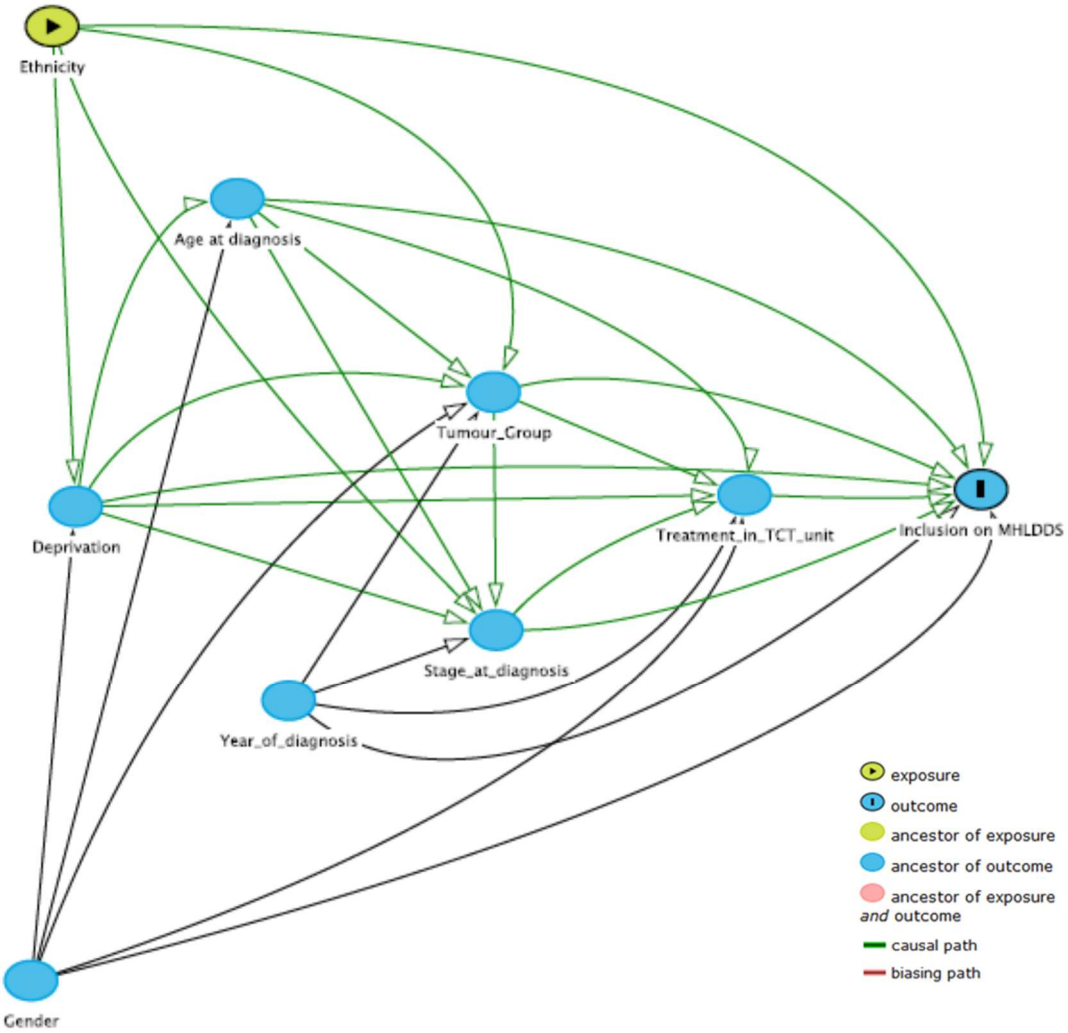


Figure C3: A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and “gender” highlighted as the primary risk factor of interest (exposure), together with all other variables.

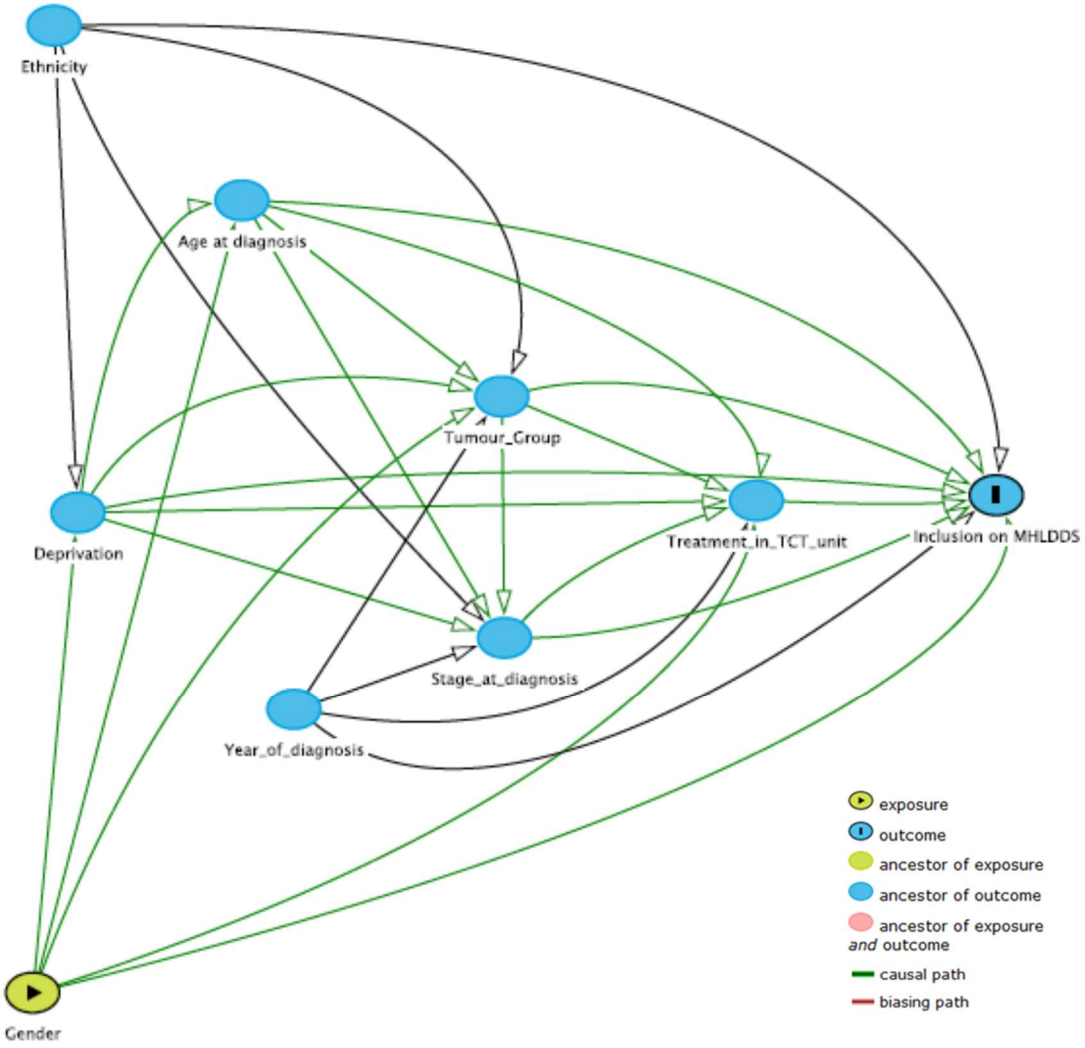


Figure C4: A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and “stage at diagnosis” highlighted as the primary risk factor of interest (exposure), together with all other variables.

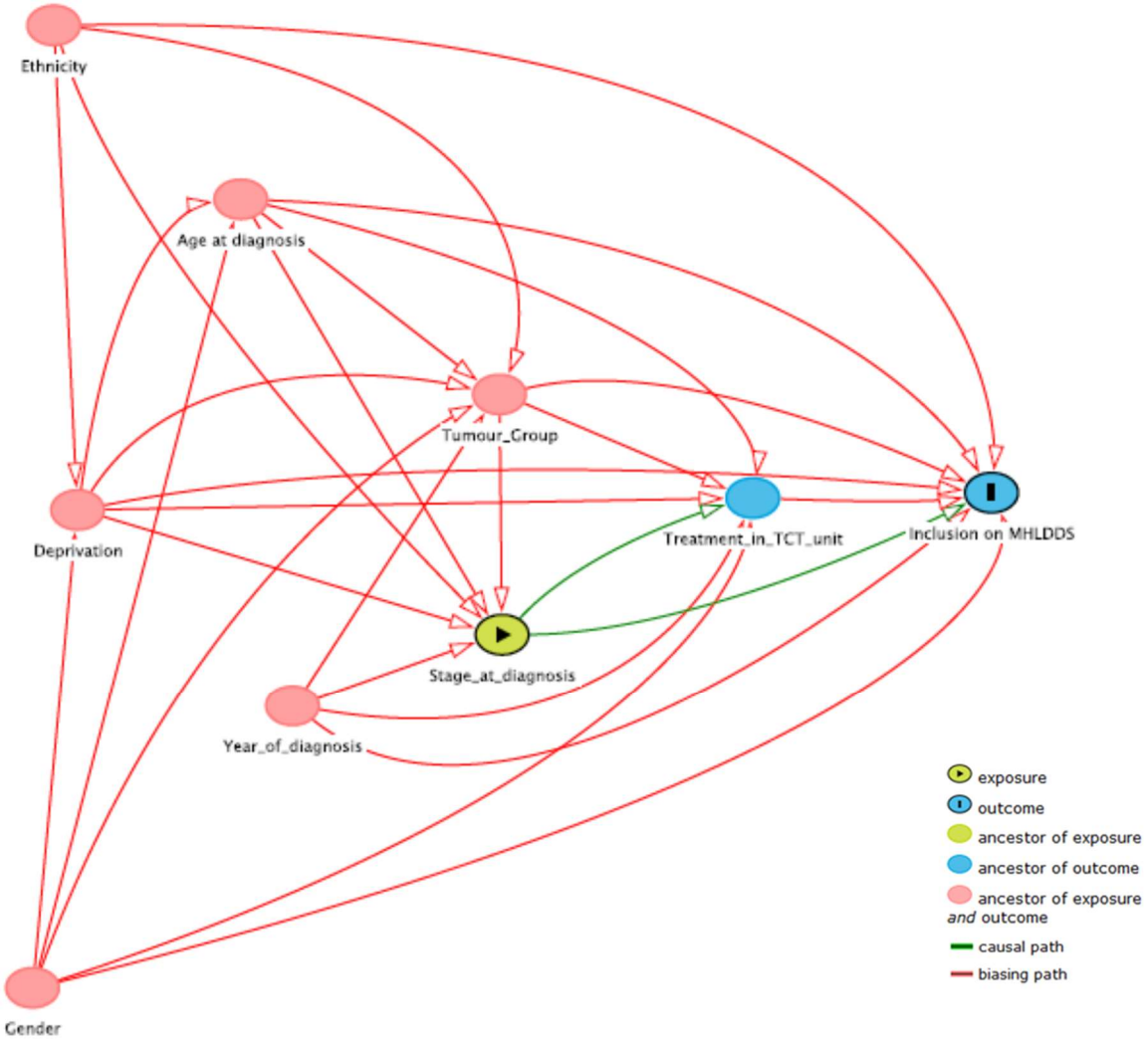


Figure C5: A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and “treatment at specialist TYA unit” highlighted as the primary risk factor of interest (exposure), together with all other variables.

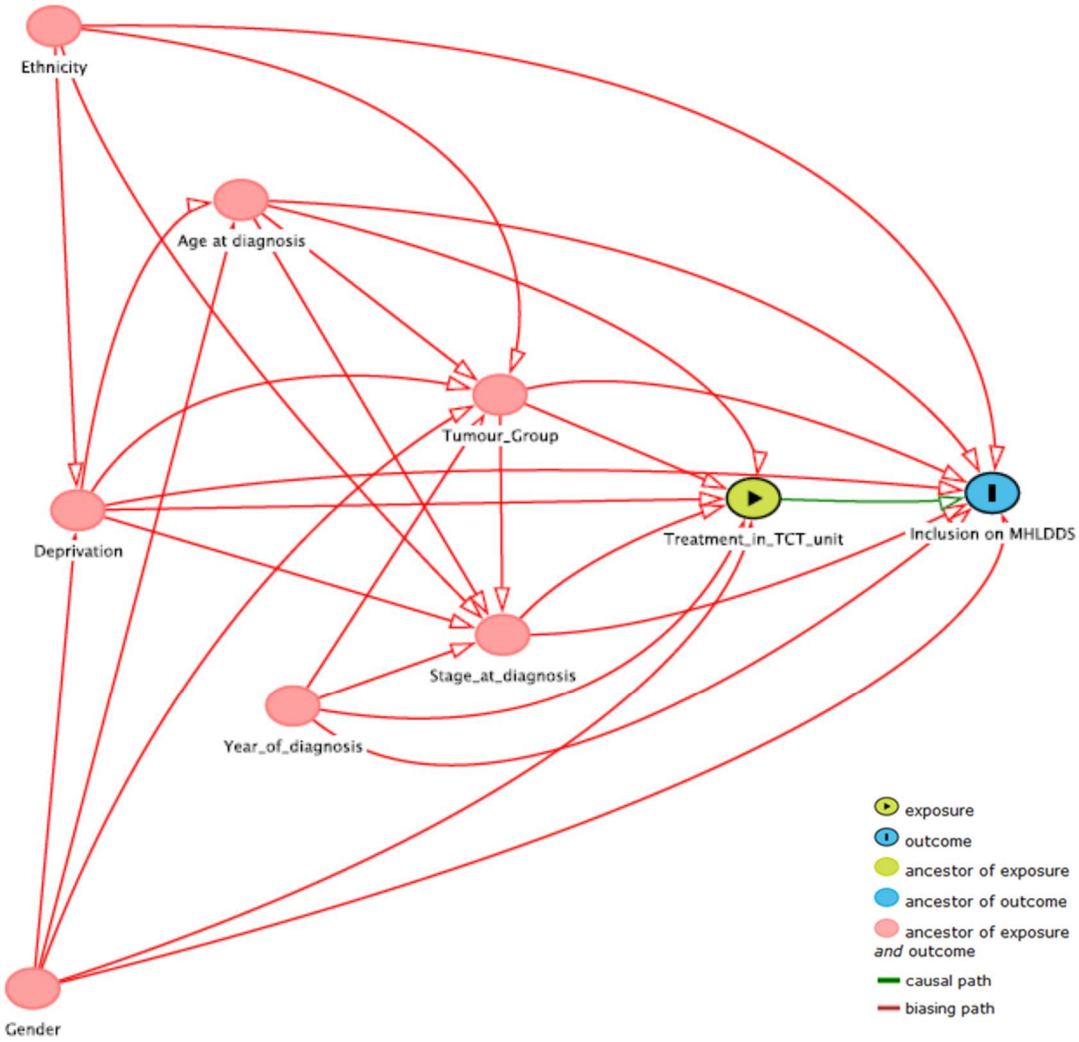


Figure C6: A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and “tumour type” highlighted as the primary risk factor of interest (exposure), together with all other variables.

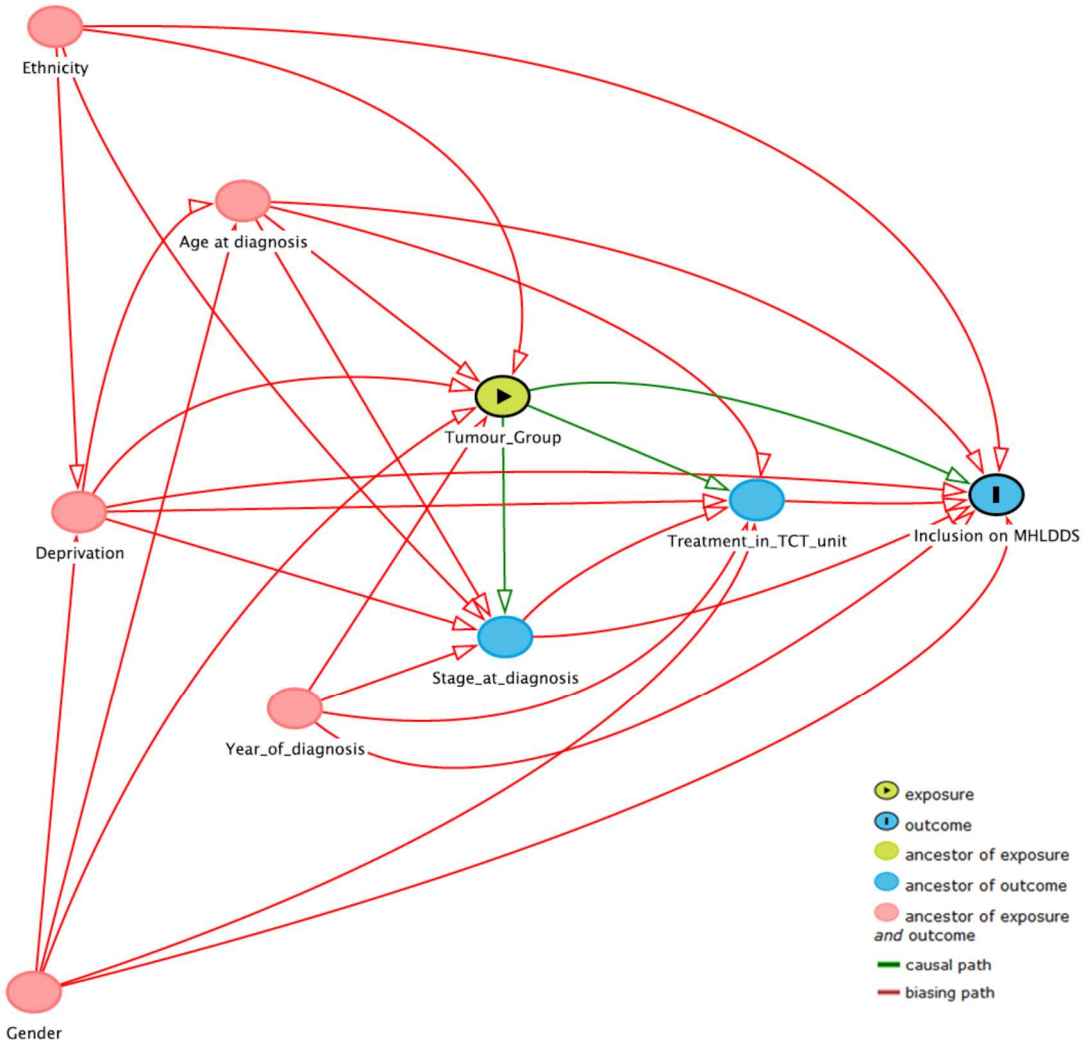
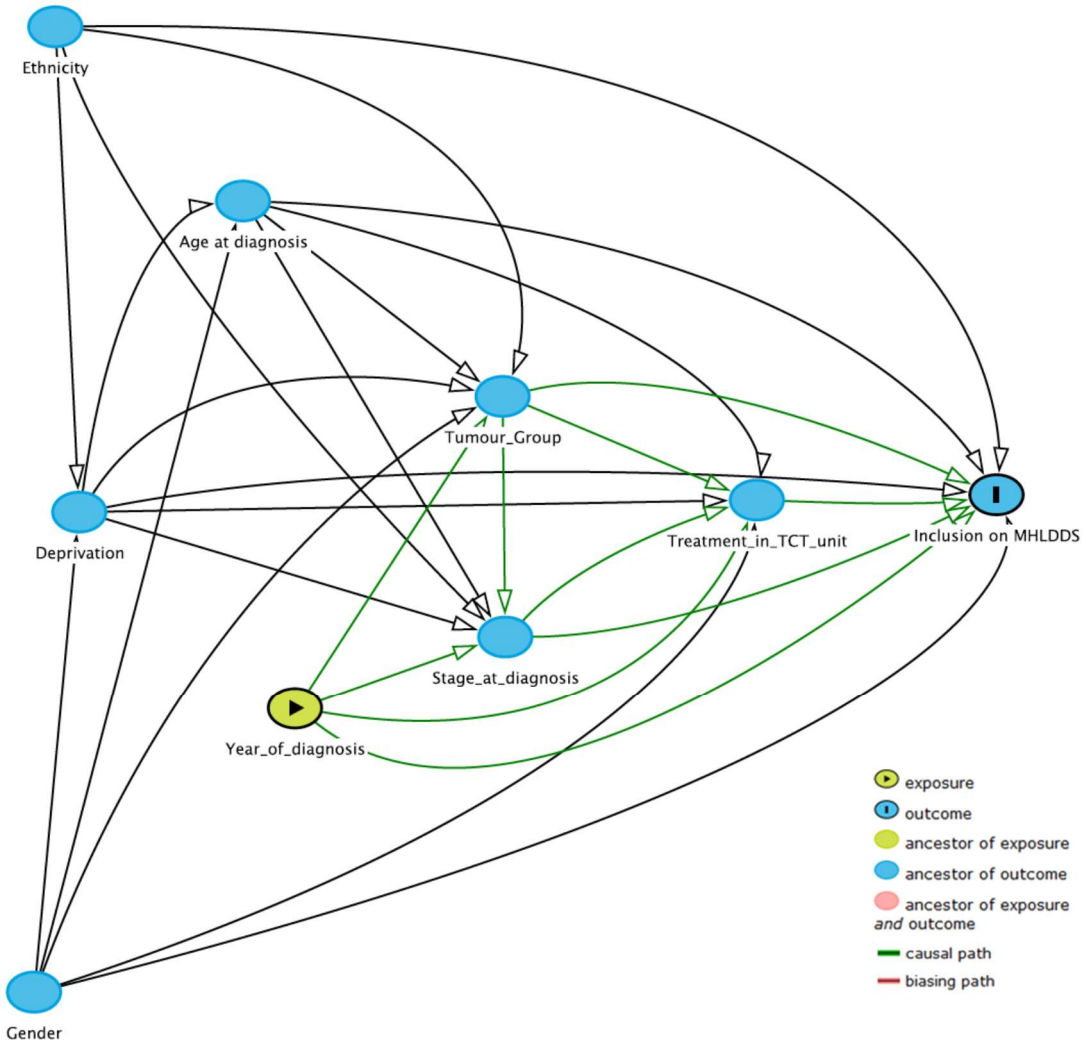


Figure C7: A Directed acyclic Graph describing the causal relationship between risk of mental health hospitalisation and “year of diagnosis” highlighted as the primary risk factor of interest (exposure), together with all other variables.



Appendix D: Mental Health Contacts Per Financial Year 2006-07 to 2015-16

This appendix gives full details of the data described in section 5.4: Comparison between Mental Health Services Use amongst Individuals on the Yorkshire Specialist Register of Cancer in Children and Young People and the Yorkshire Population as a Whole. Data in these tables are broken down by age (5 year age groups) and sex. To ensure anonymity of patients, population data was small number suppressed, so an asterisk (*) denotes fewer than 5 individuals in that specific group.

Table Da Characteristics of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire population, and number of contacts with mental health services for the financial year 2006-07.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	155287	255	285	1	164	351
Male	10 to 14	169833	350	506	2	206	395

Male	15 to 19	176746	1,535	451	11	868	2439
Male	20 to 24	188020	2,600	713	7	1383	982
Male	25 to 29	162529	3,255	745	4	2003	537
Male	30 to 34	165102	3,715	617	0	2250	0
Male	35 to 39	192276	3,885	274	0	2021	0
Male	40 to 44	195660	3,705	267	0	1894	0
Male	45 to 49	178394	3,135	24	0	1757	0
Male	50 to 54	159359	2,545	0	0	1597	-
Male	55 to 59	170719	2,485	0	0	1456	-
Female	5 to 9	149673	105	228	0	70	0
Female	10 to 14	162669	235	305	9	144	2951
Female	15 to 19	171816	1,885	381	26	1097	6824
Female	20 to 24	185259	2,915	470	25	1573	5319

Female	25 to 29	160653	3,120	468	19	1942	4060
Female	30 to 34	167326	3,545	390	18	2119	4615
Female	35 to 39	196070	4,070	274	11	2076	4015
Female	40 to 44	198015	3,975	113	5	2007	4425
Female	45 to 49	179552	3,315	18	1	1846	5556
Female	50 to 54	159385	2,815	0	0	1766	-
Female	55 to 59	173071	2,610	0	0	1508	-

Table Db Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2007-08.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	152629	20	253	2	13	791
Male	10 to 14	167718	80	396	9	48	2273
Male	15 to 19	178028	1995	473	22	1121	4651
Male	20 to 24	190703	3460	697	25	1814	3587
Male	25 to 29	169510	4285	750	21	2528	2800
Male	30 to 34	159057	4605	621	25	2895	4026
Male	35 to 39	190695	5200	514	20	2727	3891

Male	40 to 44	196751	5030	266	5	2557	1880
Male	45 to 49	181841	4245	47	1	2334	2128
Male	50 to 54	161756	3530	0	0	2182	-
Male	55 to 59	162327	3225	0	0	1987	-
Female	5 to 9	146978	10	205	0	7	0
Female	10 to 14	160760	85	283	4	53	1413
Female	15 to 19	173169	2475	364	20	1429	5495
Female	20 to 24	187645	3945	474	35	2102	7384
Female	25 to 29	167284	4320	475	12	2582	2526
Female	30 to 34	159724	4615	385	13	2889	3377
Female	35 to 39	194370	5525	312	13	2843	4167
Female	40 to 44	198929	5440	139	9	2735	6475
Female	45 to 49	183922	4760	29	0	2588	0

Female	50 to 54	161844	3890	0	0	2404	-
Female	55 to 59	164705	3585	0	0	2177	-

Table Dc Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2008-09.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	150910	5	239	2	3	837
Male	10 to 14	165492	55	362	6	33	1657
Male	15 to 19	179588	2395	448	20	1334	4464
Male	20 to 24	191194	3950	660	17	2066	2576

Male	25 to 29	175853	4655	759	17	2647	2240
Male	30 to 34	156394	4810	644	21	3076	3261
Male	35 to 39	187248	5640	559	14	3012	2504
Male	40 to 44	196919	5325	297	9	2704	3030
Male	45 to 49	185638	4540	88	1	2446	1136
Male	50 to 54	165051	3790	0	0	2296	-
Male	55 to 59	157879	3255	0	0	2062	-
Female	5 to 9	145122	*	190	1	<3	526
Female	10 to 14	159211	95	270	2	60	741
Female	15 to 19	173163	2960	351	13	1709	3704
Female	20 to 24	190667	4170	445	27	2187	6067
Female	25 to 29	172876	4620	492	17	2672	3455
Female	30 to 34	155939	4550	392	14	2918	3571

Female	35 to 39	190677	5535	354	8	2903	2260
Female	40 to 44	198375	5710	163	7	2878	4294
Female	45 to 49	187538	4970	46	1	2650	2174
Female	50 to 54	165584	4155	0	0	2509	-
Female	55 to 59	159282	3530	0	0	2216	-

Table Dd Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2009-10.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	150699	10	240	2	7	833

Male	10 to 14	163658	50	325	3	31	923
Male	15 to 19	181011	2400	432	11	1326	2546
Male	20 to 24	189068	3975	586	22	2102	3754
Male	25 to 29	176419	4365	780	15	2474	1923
Male	30 to 34	158376	4725	644	12	2983	1863
Male	35 to 39	181703	5395	612	11	2969	1797
Male	40 to 44	196070	5370	331	7	2739	2115
Male	45 to 49	189784	4690	141	3	2471	2128
Male	50 to 54	167675	3840	1	0	2290	0
Male	55 to 59	156201	3190	0	0	2042	-
Female	5 to 9	144927	*	168	1	<3	595
Female	10 to 14	157153	80	254	1	51	394
Female	15 to 19	174399	2785	324	9	1597	2778

Female	20 to 24	190457	4335	425	21	2276	4941
Female	25 to 29	174848	4430	499	13	2534	2605
Female	30 to 34	155785	4425	410	12	2840	2927
Female	35 to 39	184624	5365	378	7	2906	1852
Female	40 to 44	197932	5590	189	4	2824	2116
Female	45 to 49	191479	5010	72	4	2616	5556
Female	50 to 54	168712	4210	1	0	2495	0
Female	55 to 59	157503	3455	0	0	2194	-

Table De Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2010-11.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with	Proportion (per 100,000) of YSRCCYP Population with

						MHMDS or MHLDDS record	MHMDS or MHLDDS record
Male	5 to 9	151812	10	214	1	7	467
Male	10 to 14	161736	25	308	1	15	325
Male	15 to 19	180251	2345	430	14	1301	3256
Male	20 to 24	191756	4070	539	21	2122	3896
Male	25 to 29	175949	4285	738	13	2435	1762
Male	30 to 34	161810	4775	695	18	2951	2590
Male	35 to 39	176893	5465	623	15	3089	2408
Male	40 to 44	194540	5380	384	12	2765	3125
Male	45 to 49	193017	4905	185	6	2541	3243
Male	50 to 54	171703	3855	6	0	2245	0
Male	55 to 59	155273	3280	0	0	2112	-
Female	5 to 9	146333	5	148	1	3	676

Female	10 to 14	155789	45	238	1	29	420
Female	15 to 19	173107	2910	306	4	1681	1307
Female	20 to 24	190828	4380	419	24	2295	5728
Female	25 to 29	176440	4410	476	13	2499	2731
Female	30 to 34	159453	4490	429	15	2816	3497
Female	35 to 39	178136	5255	396	10	2950	2525
Female	40 to 44	196611	5625	233	1	2861	429
Female	45 to 49	194412	5230	84	3	2690	3571
Female	50 to 54	173153	4280	7	0	2472	0
Female	55 to 59	155741	3535	0	0	2270	-

Table Df Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2011-12.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	155272	5	201	0	3	0
Male	10 to 14	158335	30	285	1	19	351
Male	15 to 19	178838	2430	405	10	1359	2469
Male	20 to 24	196830	5590	510	14	2840	2745
Male	25 to 29	176818	5390	706	17	3048	2408
Male	30 to 34	165170	5900	740	19	3572	2568
Male	35 to 39	170345	6160	613	14	3616	2284

Male	40 to 44	194396	6830	449	10	3513	2227
Male	45 to 49	195079	6225	227	8	3191	3524
Male	50 to 54	175586	4970	24	1	2831	4167
Male	55 to 59	156029	4135	0	0	2650	-
Female	5 to 9	149374	*	136	1	<3	735
Female	10 to 14	152693	70	228	0	46	0
Female	15 to 19	172391	3265	304	8	1894	2632
Female	20 to 24	193090	6540	379	26	3387	6860
Female	25 to 29	176796	6350	469	18	3592	3838
Female	30 to 34	163631	6215	464	11	3798	2371
Female	35 to 39	170086	6330	381	10	3722	2625
Female	40 to 44	196674	7300	276	7	3712	2536
Female	45 to 49	196128	7000	111	3	3569	2703

Female	50 to 54	177520	5830	18	1	3284	5556
Female	55 to 59	156652	4720	0	0	3013	-

Table Dg Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2012-13.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	159108	105	192	0	66	0
Male	10 to 14	155203	180	253	1	116	395
Male	15 to 19	177400	2375	396	13	1339	3283
Male	20 to 24	201574	5705	472	16	2830	3390

Male	25 to 29	176774	5380	691	18	3043	2605
Male	30 to 34	168397	5635	743	18	3346	2423
Male	35 to 39	163311	5925	617	21	3628	3404
Male	40 to 44	191554	6640	511	15	3466	2935
Male	45 to 49	195772	6320	265	7	3228	2642
Male	50 to 54	179699	5325	47	2	2963	4255
Male	55 to 59	158532	4260	0	0	2687	-
Female	5 to 9	153322	30	140	1	20	714
Female	10 to 14	149604	150	204	0	100	0
Female	15 to 19	170110	3030	282	5	1781	1773
Female	20 to 24	195408	6455	363	23	3303	6336
Female	25 to 29	177270	6070	472	20	3424	4237
Female	30 to 34	168344	6060	472	16	3600	3390

Female	35 to 39	162306	5835	388	11	3595	2835
Female	40 to 44	194673	6980	308	8	3585	2597
Female	45 to 49	196790	6840	135	4	3476	2963
Female	50 to 54	181893	5815	29	1	3197	3448
Female	55 to 59	159177	4820	0	0	3028	-

Table Dh Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2013-14.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	161093	20	184	0	12	0

Male	10 to 14	150126	75	238	1	50	420
Male	15 to 19	170259	2320	362	9	1363	2486
Male	20 to 24	200000	5880	387	16	2940	4134
Male	25 to 29	175559	5695	654	16	3244	2446
Male	30 to 34	168436	5685	750	22	3375	2933
Male	35 to 39	155377	5890	641	19	3791	2964
Male	40 to 44	184123	6660	556	11	3617	1978
Male	45 to 49	191154	6630	295	14	3468	4746
Male	50 to 54	179297	5640	88	1	3146	1136
Male	55 to 59	157524	4585	0	0	2911	-
Female	5 to 9	154677	5	134	0	3	0
Female	10 to 14	144720	110	189	0	76	0
Female	15 to 19	163717	3225	268	2	1970	746

Female	20 to 24	192024	6785	350	15	3533	4286
Female	25 to 29	176174	6545	452	19	3715	4204
Female	30 to 34	169881	6440	488	18	3791	3689
Female	35 to 39	154220	5950	385	9	3858	2338
Female	40 to 44	186781	6980	352	8	3737	2273
Female	45 to 49	192575	6890	161	2	3578	1242
Female	50 to 54	181300	6195	46	3	3417	6522
Female	55 to 59	159243	5070	0	0	3184	-

Table Di Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2014-15

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	167988	40	169	0	24	0
Male	10 to 14	152590	265	235	1	174	426
Male	15 to 19	171781	3330	325	8	1939	2462
Male	20 to 24	202804	7420	430	17	3659	3953
Male	25 to 29	179330	6800	583	23	3792	3945
Male	30 to 34	171509	6540	773	23	3813	2975
Male	35 to 39	157911	6330	639	12	4009	1878

Male	40 to 44	182022	7070	609	14	3884	2299
Male	45 to 49	194112	7100	330	6	3658	1818
Male	50 to 54	187732	6340	140	3	3377	2143
Male	55 to 59	163387	5140	1	0	3146	0
Female	5 to 9	161195	15	124	0	9	0
Female	10 to 14	147039	370	168	0	252	0
Female	15 to 19	165108	4280	251	5	2592	1992
Female	20 to 24	194267	7850	324	11	4041	3395
Female	25 to 29	179142	7365	423	20	4111	4728
Female	30 to 34	174326	7075	495	18	4058	3636
Female	35 to 39	156859	6695	403	16	4268	3970
Female	40 to 44	184299	7300	315	8	3961	2540
Female	45 to 49	196669	7500	188	6	3814	3191

Female	50 to 54	189415	6940	71	3	3664	4225
Female	55 to 59	166149	5490	1	0	3304	0

Table Dj Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of contacts with mental health services for the financial year 2015-16 (partial year only).

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	171839	25	148	0	15	0
Male	10 to 14	153766	55	211	1	36	474
Male	15 to 19	170728	2985	307	1	1748	326
Male	20 to 24	201670	6790	425	5	3367	1176

Male	25 to 29	182668	6205	537	5	3397	931
Male	30 to 34	171910	5810	733	6	3380	819
Male	35 to 39	159967	5575	691	6	3485	868
Male	40 to 44	176292	6100	618	8	3460	1294
Male	45 to 49	192672	6185	382	12	3210	3141
Male	50 to 54	190939	5545	184	1	2904	543
Male	55 to 59	167866	4605	6	0	2743	0
Female	5 to 9	164525	10	120	0	6	0
Female	10 to 14	148329	115	148	1	78	676
Female	15 to 19	163858	3500	236	1	2136	424
Female	20 to 24	193226	7000	306	3	3623	980
Female	25 to 29	179938	6595	418	7	3665	1675
Female	30 to 34	175653	6150	472	4	3501	847

Female	35 to 39	160071	5720	423	6	3573	1418
Female	40 to 44	177771	6040	392	5	3398	1276
Female	45 to 49	195697	6475	233	2	3309	858
Female	50 to 54	192841	6075	83	2	3150	2410
Female	55 to 59	170980	4935	7	0	2886	0

Appendix E: Mental Health Co-Morbidity Per Financial Year 1997-98 to 2016-17

This appendix gives full details of the data described in section 5.5: Comparison between Mental Health Co-Morbidity amongst Individuals on the Yorkshire Specialist Register of Cancer in Children and Young People and the Yorkshire Population. Data in these tables are broken down by age (5 year age groups) and sex.

Table Ea Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 1997-98.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	172875	30	479	0	17	0
Male	10 to 14	164457	121	701	1	74	143
Male	15 to 19	153988	499	752	0	324	0

Male	20 to 24	156350	1,014	625	2	649	320
Male	25 to 29	179797	1,104	521	2	614	384
Male	30 to 34	190822	1,020	274	2	535	730
Male	35 to 39	178780	926	47	0	518	0
Male	40 to 44	160788	499	0	0	310	0
Female	5 to 9	165852	11	368	0	7	0
Female	10 to 14	156937	94	477	0	60	0
Female	15 to 19	149528	498	478	0	333	0
Female	20 to 24	152605	699	400	2	458	500
Female	25 to 29	181367	819	316	0	385	0
Female	30 to 34	194057	909	143	0	422	0
Female	35 to 39	181294	761	31	0	501	0
Female	40 to 44	161112	681	0	0	472	0

Table Eb Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 1998-99.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	171797	46	451	0	27	0
Male	10 to 14	167233	207	665	0	124	0
Male	15 to 19	155948	740	764	0	475	0
Male	20 to 24	150378	1340	646	2	891	310
Male	25 to 29	175072	1492	570	0	852	0
Male	30 to 34	189141	1453	303	5	768	1650

Male	35 to 39	182078	1331	89	2	731	2247
Male	40 to 44	163527	1151	0	0	704	0
Female	5 to 9	165852	164038	9	353	15	0
Female	10 to 14	156937	159654	104	449	166	2
Female	15 to 19	149528	151359	464	495	703	2
Female	20 to 24	152605	147161	610	396	898	2
Female	25 to 29	181367	177037	595	361	1054	0
Female	30 to 34	194057	192628	588	167	1132	0
Female	35 to 39	181294	184516	572	49	1056	0
Female	40 to 44	161112	164436	545	0	896	0

Table Ec Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 1999-2000.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	170305	52	434	0	31	0
Male	10 to 14	168947	235	592	2	139	338
Male	15 to 19	158069	818	786	2	517	254
Male	20 to 24	149566	1313	646	3	878	464
Male	25 to 29	165670	1456	621	1	879	161
Male	30 to 34	186171	1420	337	1	763	297
Male	35 to 39	184315	1288	145	0	699	0

Male	40 to 44	166019	1118	1	0	673	0
Female	5 to 9	162796	21	325	0	13	0
Female	10 to 14	162148	214	430	0	132	0
Female	15 to 19	154542	647	502	0	419	0
Female	20 to 24	146763	765	415	1	521	241
Female	25 to 29	169112	847	387	1	501	258
Female	30 to 34	189959	978	194	0	515	0
Female	35 to 39	188074	975	194	0	518	0
Female	40 to 44	167348	948	74	0	566	0

Table Ed Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2000-01.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	167546	54	432	0	32	0
Male	10 to 14	169929	193	545	0	114	0
Male	15 to 19	160085	795	746	1	497	134
Male	20 to 24	149711	1,332	700	3	890	429
Male	25 to 29	158937	1,535	631	3	966	475
Male	30 to 34	182967	1,513	389	3	827	771
Male	35 to 39	186511	1,553	189	2	833	1058

Male	40 to 44	169753	1,203	6	0	709	0
Female	5 to 9	159686	13	308	0	8	0
Female	10 to 14	163310	212	424	0	130	0
Female	15 to 19	155011	602	478	4	388	837
Female	20 to 24	149181	824	436	1	552	229
Female	25 to 29	162858	1,002	406	0	615	0
Female	30 to 34	188007	953	238	0	507	0
Female	35 to 39	190943	1,261	87	0	660	0
Female	40 to 44	171459	996	7	0	581	0

Table Ee Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2001-02.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	164178	63	406	0	38	0
Male	10 to 14	171854	210	515	1	122	194
Male	15 to 19	163711	724	716	2	442	279
Male	20 to 24	153034	1230	154	7	804	4545
Male	25 to 29	151923	1510	621	6	994	966
Male	30 to 34	181755	1599	456	1	880	219
Male	35 to 39	188097	1571	228	0	835	0

Male	40 to 44	173558	1361	24	0	784	0
Female	5 to 9	156839	23	305	0	15	0
Female	10 to 14	165354	214	384	0	129	0
Female	15 to 19	157813	577	471	2	366	425
Female	20 to 24	154001	824	471	5	535	1062
Female	25 to 29	156249	937	392	2	600	510
Female	30 to 34	187561	1046	281	0	558	0
Female	35 to 39	192490	1182	115	0	614	0
Female	40 to 44	175852	1115	19	0	634	0

Table Ef Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2002-03.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	165074	63	396	0	38	0
Male	10 to 14	175138	173	477	1	99	210
Male	15 to 19	170083	695	700	0	409	0
Male	20 to 24	161830	1279	752	3	790	399
Male	25 to 29	148244	1602	624	2	1081	321
Male	30 to 34	182911	1813	518	0	991	0
Male	35 to 39	193480	1698	268	0	878	0

Male	40 to 44	181624	1441	47	1	793	2128
Female	5 to 9	157965	14	283	0	9	0
Female	10 to 14	168847	188	366	0	111	0
Female	15 to 19	163361	672	475	2	411	421
Female	20 to 24	164822	886	476	2	538	420
Female	25 to 29	151920	987	398	1	650	251
Female	30 to 34	190095	1181	315	1	621	317
Female	35 to 39	198154	1261	141	0	636	0
Female	40 to 44	184138	1175	30	0	638	0

Table Eg Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2003-04.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	162947	67	362	1	41	276
Male	10 to 14	174125	223	450	1	128	222
Male	15 to 19	173536	635	662	0	366	0
Male	20 to 24	168427	1372	763	3	815	393
Male	25 to 29	144840	1544	646	5	1066	774
Male	30 to 34	179062	1772	565	1	990	177
Male	35 to 39	193556	1782	299	2	921	669

Male	40 to 44	185654	1583	88	0	853	0
Female	5 to 9	156660	15	270	0	10	0
Female	10 to 14	167375	220	351	1	131	285
Female	15 to 19	167955	593	447	0	353	0
Female	20 to 24	171591	938	493	4	547	811
Female	25 to 29	148205	986	394	1	665	254
Female	30 to 34	186623	1210	359	1	648	279
Female	35 to 39	197992	1293	166	0	653	0
Female	40 to 44	188249	1218	47	1	647	2128

Table Eh Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2004-05.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	161285	84	325	0	52	0
Male	10 to 14	173880	226	433	1	130	231
Male	15 to 19	174545	741	589	2	425	340
Male	20 to 24	178294	1261	785	2	707	255
Male	25 to 29	148412	1513	646	3	1019	464
Male	30 to 34	174828	1836	617	2	1050	324
Male	35 to 39	193215	1900	334	1	983	299

Male	40 to 44	190067	1717	142	1	903	704
Female	5 to 9	154826	20	254	0	13	0
Female	10 to 14	166436	260	325	0	156	0
Female	15 to 19	169637	688	428	2	406	467
Female	20 to 24	176551	993	500	2	562	400
Female	25 to 29	149169	1069	413	1	717	242
Female	30 to 34	180559	1233	385	0	683	0
Female	35 to 39	197713	1359	193	0	687	0
Female	40 to 44	192880	1717	73	0	890	0

Table Ei Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2005-06.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	158967	67	308	1	42	325
Male	10 to 14	172505	220	431	2	128	464
Male	15 to 19	175352	741	542	0	423	0
Male	20 to 24	185633	1381	745	1	744	134
Male	25 to 29	156791	1569	700	4	1001	571
Male	30 to 34	171243	1812	626	1	1058	160
Male	35 to 39	193120	1922	384	2	995	521

Male	40 to 44	194136	1870	187	1	963	535
Female	5 to 9	152994	22	238	0	14	0
Female	10 to 14	164583	272	308	1	165	325
Female	15 to 19	171115	658	422	4	385	948
Female	20 to 24	182278	1067	476	0	585	0
Female	25 to 29	154961	1069	433	4	690	924
Female	30 to 34	174863	1380	405	3	789	741
Female	35 to 39	196412	1405	237	0	715	0
Female	40 to 44	196407	1517	86	0	772	0

Table Ej Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2006-07.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	155287	86	285	0	55	0
Male	10 to 14	169833	279	506	2	164	395
Male	15 to 19	176746	767	451	3	434	665
Male	20 to 24	188020	1358	713	3	722	421
Male	25 to 29	162529	1630	745	2	1003	268
Male	30 to 34	165102	1891	617	4	1145	648
Male	35 to 39	192276	2037	274	2	1059	730
Male	40 to 44	195660	1964	267	0	1004	0

Female	5 to 9	149673	21	228	0	14	0
Female	10 to 14	162669	259	305	0	159	0
Female	15 to 19	171816	723	381	2	421	525
Female	20 to 24	185259	1095	470	1	591	213
Female	25 to 29	160653	1239	468	0	771	0
Female	30 to 34	167326	1289	390	4	770	1026
Female	35 to 39	196070	1490	274	0	760	0
Female	40 to 44	198015	1664	113	1	840	885

Table Ek Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2007-08.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	152629	97	253	0	64	0
Male	10 to 14	167718	230	396	0	137	0
Male	15 to 19	178028	755	473	1	424	211
Male	20 to 24	190703	1202	697	2	630	287
Male	25 to 29	169510	1599	750	4	943	533
Male	30 to 34	159057	1740	621	1	1094	161
Male	35 to 39	190695	2019	514	1	1059	195

Male	40 to 44	196751	2129	266	0	1082	0
Female	5 to 9	146978	31	205	0	21	0
Female	10 to 14	160760	295	283	0	184	0
Female	15 to 19	173169	698	364	4	403	1099
Female	20 to 24	187645	1085	474	2	578	422
Female	25 to 29	167284	1316	475	2	787	421
Female	30 to 34	159724	1370	385	4	858	1039
Female	35 to 39	194370	1479	312	1	761	321
Female	40 to 44	198929	1604	139	0	806	0

Table EI Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2008-09.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	150910	127	239	1	84	418
Male	10 to 14	165492	300	362	1	181	276
Male	15 to 19	179588	765	448	4	426	893
Male	20 to 24	191194	1311	660	4	686	606
Male	25 to 29	175853	1621	759	4	922	527
Male	30 to 34	156394	1893	644	1	1210	155
Male	35 to 39	187248	2227	559	3	1189	537

Male	40 to 44	196919	2334	297	0	1185	0
Female	5 to 9	145122	81	190	1	56	526
Female	10 to 14	159211	290	270	0	182	0
Female	15 to 19	173163	795	351	4	459	1140
Female	20 to 24	190667	1185	445	5	622	1124
Female	25 to 29	172876	1412	492	2	817	407
Female	30 to 34	155939	1384	392	3	888	765
Female	35 to 39	190677	1743	354	2	914	565
Female	40 to 44	198375	1915	163	0	965	0

Table Em Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2009-10.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	150699	121	240	1	80	417
Male	10 to 14	163658	316	325	1	193	308
Male	15 to 19	181011	835	432	2	461	463
Male	20 to 24	189068	1512	586	3	800	512
Male	25 to 29	176419	1866	780	4	1058	513
Male	30 to 34	158376	2108	644	2	1331	311
Male	35 to 39	181703	2488	612	3	1369	490

Male	40 to 44	196070	2727	331	1	1391	302
Male	45 to 49	189784	544	141	4	287	2837
Female	5 to 9	144927	85	168	0	59	0
Female	10 to 14	157153	332	254	2	211	787
Female	15 to 19	174399	1067	324	3	612	926
Female	20 to 24	190457	1621	425	3	851	706
Female	25 to 29	174848	1822	499	6	1042	1202
Female	30 to 34	155785	1779	410	5	1142	1220
Female	35 to 39	184624	2079	378	0	1126	0
Female	40 to 44	197932	2217	189	0	1120	0
Female	45 to 49	191479	386	72	0	202	0

Table En Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2010-11.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	151812	193	214	1	127	467
Male	10 to 14	161736	342	308	2	211	649
Male	15 to 19	180251	1058	430	5	587	1163
Male	20 to 24	191756	1860	539	7	970	1299
Male	25 to 29	175949	2254	738	3	1281	407
Male	30 to 34	161810	2613	695	6	1615	863
Male	35 to 39	176893	3260	623	4	1843	642

Male	40 to 44	194540	3405	384	3	1750	781
Male	45 to 49	193017	657	185	0	340	0
Female	5 to 9	146333	143	148	2	98	1351
Female	10 to 14	155789	362	238	1	232	420
Female	15 to 19	173107	1296	306	1	749	327
Female	20 to 24	190828	2196	419	7	1151	1671
Female	25 to 29	176440	2383	476	3	1351	630
Female	30 to 34	159453	2459	429	5	1542	1166
Female	35 to 39	178136	2807	396	6	1576	1515
Female	40 to 44	196611	3058	233	2	1555	858
Female	45 to 49	194412	604	84	0	311	0

Table Eo Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2011-12.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	155272	180	201	1	116	498
Male	10 to 14	158335	373	285	6	236	2105
Male	15 to 19	178838	2047	405	3	1145	741
Male	20 to 24	196830	4448	510	14	2260	2745
Male	25 to 29	176818	4723	706	19	2671	2691
Male	30 to 34	165170	4963	740	12	3005	1622
Male	35 to 39	170345	5947	613	9	3491	1468

Male	40 to 44	194396	6872	449	9	3535	2004
Male	45 to 49	195079	5855	227	3	3001	1322
Male	50 to 54	175586	5222	24	0	2974	0
Male	55 to 59	156029	4833	0	0	3098	0
Female	5 to 9	149374	112	136	0	75	0
Female	10 to 14	152693	439	228	0	288	0
Female	15 to 19	172391	4071	304	2	2361	658
Female	20 to 24	193090	7836	379	12	4058	3166
Female	25 to 29	176796	7074	469	16	4001	3412
Female	30 to 34	163631	5944	464	12	3633	2586
Female	35 to 39	170086	5951	381	10	3499	2625
Female	40 to 44	196674	6540	276	4	3325	1449
Female	45 to 49	196128	6022	111	1	3070	901

Female	50 to 54	177520	5151	18	0	2902	0
Female	55 to 59	156652	4254	0	0	2716	0

Table Ep Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2012-13.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	159108	201	192	1	126	521
Male	10 to 14	155203	339	253	1	218	395
Male	15 to 19	177400	2323	396	9	1309	2273
Male	20 to 24	201574	5127	472	20	2543	4237

Male	25 to 29	176774	5310	691	11	3004	1592
Male	30 to 34	168397	5975	743	6	3548	808
Male	35 to 39	163311	6411	617	10	3926	1621
Male	40 to 44	191554	7703	511	2	4021	391
Male	45 to 49	195772	7568	265	2	3866	755
Male	50 to 54	179699	7294	47	0	4059	0
Male	55 to 59	158532	6416	0	0	4047	0
Female	5 to 9	153322	101	140	1	66	714
Female	10 to 14	149604	417	204	0	279	0
Female	15 to 19	170110	4857	282	10	2855	3546
Female	20 to 24	195408	9899	363	10	5066	2755
Female	25 to 29	177270	9244	472	9	5215	1907
Female	30 to 34	168344	7586	472	12	4506	2542

Female	35 to 39	162306	6690	388	7	4122	1804
Female	40 to 44	194673	7967	308	6	4093	1948
Female	45 to 49	196790	8057	135	2	4094	1481
Female	50 to 54	181893	7593	29	0	4174	0
Female	55 to 59	159177	6084	0	0	3822	0

Table Eq Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2013-14.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	161093	203	184	2	126	1087

Male	10 to 14	150126	394	238	0	262	0
Male	15 to 19	170259	2462	362	7	1446	1934
Male	20 to 24	200000	5413	387	6	2707	1550
Male	25 to 29	175559	6025	654	12	3432	1835
Male	30 to 34	168436	6437	750	8	3822	1067
Male	35 to 39	155377	6523	641	12	4198	1872
Male	40 to 44	184123	7917	556	8	4300	1439
Male	45 to 49	191154	7939	295	5	4153	1695
Male	50 to 54	179297	7993	88	1	4458	1136
Male	55 to 59	157524	7154	0	0	4542	0
Female	5 to 9	154677	125	134	1	81	746
Female	10 to 14	144720	509	189	1	352	529
Female	15 to 19	163717	5151	268	7	3146	2612

Female	20 to 24	192024	11023	350	10	5740	2857
Female	25 to 29	176174	10182	452	17	5780	3761
Female	30 to 34	169881	8752	488	6	5152	1230
Female	35 to 39	154220	7051	385	5	4572	1299
Female	40 to 44	186781	8474	352	10	4537	2841
Female	45 to 49	192575	8813	161	1	4576	621
Female	50 to 54	181300	8266	46	0	4559	0
Female	55 to 59	159243	6906	0	0	4337	0

Table Er Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2014-15.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with	Proportion (per 100,000) of YSRCCYP Population with

						MHMDS or MHLDDS record	MHMDS or MHLDDS record
Male	5 to 9	167988	220	169	2	131	1183
Male	10 to 14	152590	416	235	3	273	1277
Male	15 to 19	171781	2520	325	4	1467	1231
Male	20 to 24	202804	5683	430	5	2802	1163
Male	25 to 29	179330	6296	583	14	3511	2401
Male	30 to 34	171509	6577	773	8	3835	1035
Male	35 to 39	157911	6704	639	9	4245	1408
Male	40 to 44	182022	8188	609	8	4498	1314
Male	45 to 49	194112	8779	330	10	4523	3030
Male	50 to 54	187732	8591	140	2	4576	1429
Male	55 to 59	163387	7499	1	0	4590	0
Female	5 to 9	161195	146	124	0	91	0

Female	10 to 14	147039	513	168	1	349	595
Female	15 to 19	165108	5359	251	6	3246	2390
Female	20 to 24	194267	11361	324	7	5848	2160
Female	25 to 29	179142	11108	423	5	6201	1182
Female	30 to 34	174326	9839	495	10	5644	2020
Female	35 to 39	156859	7698	403	2	4908	496
Female	40 to 44	184299	9062	315	11	4917	3492
Female	45 to 49	196669	9568	188	4	4865	2128
Female	50 to 54	189415	9315	71	0	4918	0
Female	55 to 59	166149	7719	1	0	4646	0

Table Es Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the financial year 2015-16.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	171839	263	148	0	153	0
Male	10 to 14	153766	437	211	0	284	0
Male	15 to 19	170728	2450	307	0	1435	0
Male	20 to 24	201670	5675	425	4	2814	941
Male	25 to 29	182668	6403	537	6	3505	1117
Male	30 to 34	171910	6854	733	10	3987	1364
Male	35 to 39	159967	6611	691	10	4133	1447

Male	40 to 44	176292	7989	618	7	4532	1133
Male	45 to 49	192672	8918	382	5	4629	1309
Male	50 to 54	190939	8631	184	0	4520	0
Male	55 to 59	167866	8099	6	0	4825	0
Female	5 to 9	164525	196	120	0	119	0
Female	10 to 14	148329	535	148	0	361	0
Female	15 to 19	163858	5282	236	2	3224	847
Female	20 to 24	193226	11665	306	9	6037	2941
Female	25 to 29	179938	11874	418	8	6599	1914
Female	30 to 34	175653	10198	472	8	5806	1695
Female	35 to 39	160071	8200	423	8	5123	1891
Female	40 to 44	177771	8991	392	12	5058	3061
Female	45 to 49	195697	9871	233	1	5044	429

Female	50 to 54	192841	10073	83	2	5223	2410
Female	55 to 59	170980	8344	7	0	4880	0

Table Et Populations of the Yorkshire Specialist Register of Cancer in Children and Young People and Yorkshire and number of recorded mental health diagnoses on inpatient Hospital Episode Statistics for the partial financial year 2016-17.

Sex	Age	Yorkshire Population	Yorkshire Population with MHMDS or MHLDDS record	YSRCCYP Population	YSRCCYP Population with MHMDS or MHLDDS record	Proportion (per 100,000) of Yorkshire Population with MHMDS or MHLDDS record	Proportion (per 100,000) of YSRCCYP Population with MHMDS or MHLDDS record
Male	5 to 9	5 to 9	171383	165	117	283	2
Male	10 to 14	10 to 14	154781	279	199	432	1
Male	15 to 19	15 to 19	164448	1470	284	2417	3
Male	20 to 24	20 to 24	197034	2876	402	5667	4

Male	25 to 29	25 to 29	185133	3738	506	6921	9
Male	30 to 34	30 to 34	170656	4093	704	6985	13
Male	35 to 39	35 to 39	160032	4440	734	7106	13
Male	40 to 44	40 to 44	165352	4828	611	7983	11
Male	45 to 49	45 to 49	188542	4751	446	8957	5
Male	50 to 54	50 to 54	188456	4884	224	9204	2
Male	55 to 59	55 to 59	168292	5000	24	8414	0
Female	5 to 9	5 to 9	163594	81	93	132	0
Female	10 to 14	10 to 14	148740	361	136	537	0
Female	15 to 19	15 to 19	158176	3537	227	5595	4
Female	20 to 24	20 to 24	188347	6689	303	12598	3
Female	25 to 29	25 to 29	179967	7410	378	13336	18
Female	30 to 34	30 to 34	173525	6519	467	11312	10

Female	35 to 39	35 to 39	161104	5638	459	9083	10
Female	40 to 44	40 to 44	166626	5418	407	9028	10
Female	45 to 49	45 to 49	191763	5543	276	10629	6
Female	50 to 54	50 to 54	190431	5592	110	10648	1
Female	55 to 59	55 to 59	171507	5437	18	9325	0