Using Routine Health Data to Assess Health Outcomes in the Transitional Care Period for Individuals Diagnosed with a Long-Term Condition in Childhood or Young Adulthood.

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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.

Chapter 4 contains work based on the following publications:

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Evans-Cheung, T.C., Bodansky H.J., Parslow R.C., Feltbower, R.G. Early deaths from ischaemic heart disease in childhood-onset type 1 diabetes. Archives of Disease in Childhood. 2018; 103:981-983.

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Abstract.

Clinical guidelines surrounding transition from paediatric to adult health services are based on qualitative research. This study assessed whether routine datasets could provide empirical evidence for the need of transitional health care. Health outcomes were analysed for individuals diagnosed with type 1 diabetes (T1D) or cancer in childhood (under 15 years) or young adulthood (15 to 29 years) with up to 35 years of follow-up time, including mortality in the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) using death certification data, HbA1c levels and hospitalisations for individuals receiving Continuous Subcutaneous Insulin Infusion (CSII) therapy in the Leeds Children and Young People's Diabetes Service (LCYPDS) and hospitalisations in the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) using hospital episode statistics.

Analysis from the YRDCYP showed evidence for higher mortality during the transitional care period due to diabetic ketoacidosis. Individuals diagnosed with T1D during the transitional care period (15 to 29 years) had higher mortality rates compared with those diagnosed in childhood. CSII therapy for T1D was found to significantly reduce HbA1c values for up to 4 years in the LCYPDS, indicating it is an effective treatment option for managing T1D during the transitional care period.

In the YSRCCYP, a previous mental health admission increased the odds of an A&E attendance and non-attendance to an outpatient appointment. There was evidence of poorer adherence during the transitional care period compared with younger age groups. Attending an outpatient appointment increased the odds of an inpatient admission by 50%, suggesting that missing an outpatient appointment could lead to less opportunity for referral for an inpatient admission.

Previous research into transition focused on ages under 25 years. This study showed that individuals over this age should not be overlooked. Socio-demographic factors should also be considered for targeted interventions.

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Abbreviations.

A&E	Accident and Emergency
ASD	Autistic Spectrum Disorder
AYA	Adolescent and Young Adult
BCCSS	British Childhood Cancer Survivor Study
CCSS	Childhood Cancer Survivor Study
CIPS	Continuous Inpatient Spell
CNS	Central Nervous System
CSII	Continuous Subcutaneous Insulin Infusion
CVD	Cardiovascular disease
CYA	Childhood and Young Adult
DAG	Directed Acyclic Graph
DCCT	Diabetes Control and Complications Trial
DKA	DKA: Diabetic Ketoacidosis
ICCC	International Classification of Childhood Cancer
ICD	International Classification of Diseases
IHD	Ischaemic Heart Disease
LCYPDS	Leeds Children and Young People's Diabetes Service
LTC	Long-term Condition
MDI	Multiple Daily Injections
MHMDS	Mental Health Minimum Data set
NDA	National Diabetes Audit
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NPDA	National Paediatric Diabetes Audit
NS-CSHCN	National Survey of Children with Special Health Care Needs
ONS	Office for National Statistics
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
PTSD	Post-traumatic Stress Disorder
SMR	Standardised Mortality Ratio
SQL	Structured Query Language
T1D	Type 1 Diabetes
YRDCYP	Yorkshire Registry for Diabetes in Children and Young People
YRHA	Yorkshire Regional Health Authority
YSRCCYP	Yorkshire Specialist Register of Cancer in Children and Young People

Chapter 1 Introduction.

In England, around 15 million people suffer from a long-term condition (LTC), requiring routine surveillance and management (1). LTCs create a major burden on the healthcare system, costing the National Health Service (NHS) around 70% of total expenditure (2). The majority of LTCs occur in older people, where 58% of people over 60 have at least one LTC (3). However, LTCs do not just occur in the older population. LTCs with childhood onset include asthma, epilepsy, cystic fibrosis, childhood cancer and type 1 diabetes (T1D). According to the General Lifestyle Survey, the percentage of under 15-year olds with a long-standing illness increased by around 5 to 6% between 1972 and 2011. Around a fifth of all people reporting an LTC in England are under 16 years old (3). These children and young people are typically treated in paediatric services. As they grow older, due to the organisational structure of the healthcare system, these young people will eventually have their care transferred into adult services. This time of changeover coincides with multiple life transitions, forming part of an overarching multidisciplinary transitional care period.

This thesis examined health outcomes from two LTCs – childhood and young adult (CYA) cancer and type 1 diabetes, with a focus on the transitional care period.

1.1 Defining the transitional care period.

Adolescents and young adults (AYAs) with LTCs need to transform from being a passive receiver of healthcare, where primary responsibility is placed on parents/caregivers in paediatric services, to become fully engaged participants within adult health services, where there is an expectation that the patient has the necessary skills and knowledge to self-manage their condition with a reduced level of support (4–6). This is an extensive discrete change in environment, culture and relationships with health professionals, requiring major adjustment. Experiencing this change as a one-off transfer event may be a struggle for some young people, leading to non-adherence with treatment and non-attendance at scheduled appointments which could consequently have a detrimental effect on their health. Instead, expert consensus suggest undergoing a gradual process to provide continuity of care between paediatric and adult services which is “uninterrupted, coordinated, developmentally appropriate, psychosocially sound, and comprehensive” (7, p.570), requiring a

multidisciplinary outlook including non-health related spheres such as education, employment, mental health and social services (8). This reflects recent legislation, such as the Children and Families Act 2014, towards integrating services to provide support for the 'whole child' as opposed to a single focus approach (9,10).

Assessing the outcomes of all multidisciplinary interventions involved during the transitional care period at a population level is challenging, particularly when interventions are non-standardised and implemented according to individual needs. In this study, an age group (15 to 29 years) was used as a proxy measure for the transitional care period, coinciding with the age of late CYA cancer and T1D onset. This age group was used as it includes the typical age range of the transfer event from 16 (the age of consent to a medical procedure without parental involvement) to 25 years (the upper age covered by the Children and Families Act 2014), with a minimum of one year of preparation before the transfer event and a minimum period of four years in adult services. This longer period of follow-up in adult services was included to capture the later period of 'emerging adulthood'.

Emerging adulthood describes the period after adolescence where the full social status of adulthood is yet to be achieved, despite reaching the legal adult age (11). For example, in England and Wales, 1.87 million 18 to 24-year olds are in full-time education, so are likely to be reliant on family members for financial support (12). Parental financial support can also remain for older age groups due to rising living costs, with 1 in 4 young adults aged 20 to 34-year olds still living at home (12). This means that parental involvement is present in everyday life for many young adults, making this age group distinct from older adults as they lack the experience and skills of complete independence. For AYAs with an LTC who still rely on parental support, exclusion of family members during appointments in adult services where parental involvement is no longer the norm can cause stress and anxiety, leading to negative health outcomes. Even when AYAs are living fully independently from family members, recent advances in brain imaging technology have found that the pre-frontal cortex and limbic system are still developing into the mid to the late twenties. These areas of the brain are connected to emotions, motivation, decision-making and suppression of risk-taking behaviours (13,14). This can have important effects on the self-management of an LTC in the AYA population, as they may not have the necessary mental capacity to make the right decisions to maintain optimal healthcare. For example, for an AYA with T1D, they may be more likely to be motivated by peer approval (a short-term gain) to miss insulin injections, despite risking diabetic ketoacidosis (DKA) and longer-term

complications. This neurological distinction from older adults places greater emphasis on the importance of including emerging adulthood in research regarding the transitional care period (15).

1.2 The need for empirical evidence on transitional health care.

At present, there is wide variation in delivery of specialist services during the transitional care period. For CYA cancer survivors, there is a national model of care services in England, where 16 to 18-year olds are admitted to specialist Teenage and Young Adult Principal Treatment Centres. For 19 to 24-year olds, they are given a choice of entering a Teenage and Young Adult Principal Treatment Centre or they can enter adult services directly (16,17). In contrast, although there are some services dedicated to providing transitional services for the AYA T1D population, this is not standard across England and Wales in the same way that Principal Treatment Centres exist for cancer. An increase in children surviving LTCs into adulthood will mean that this population of AYA patients will increase, placing larger demand for services during the transitional care period. In global comparisons, the UK and Australia are the only two countries with published government documentation on supported transition strategies. The Transition support programme provided funding between 2008 to 2011 to 11 NHS regions in England to develop transition systems, alongside the appointment of a National Clinical Director for Children, Young People and Transition to Adulthood. Standardised clinical guidance on transition was introduced in 2016 (18), showing that the UK government has acknowledged the importance of improving health care during the transitional care period (19).

However, the evidence base for clinical guidelines, policy and recommendations on transition largely come from qualitative interview data and surveys from health professionals, patients or family members. Empirical research into whether providing specialist care is actually needed during the transitional care period is sparse (20,21). This is problematic as specialised transitional health care is resource intensive, so there needs to be quantifiable measures to provide justification for funding these services. In this study, health outcomes during the transitional care period were compared with health outcomes before and after the transitional care period. It was hypothesised than an increase in negative health outcomes (i.e. complications or death) during the transitional care period would provide evidence to support the need of specialist care in this age group.

Empirical research can also determine whether specific sections of the patient population have greater needs for transitional health care. This provides useful

information for deciding where funding and resources should be allocated and whether interventions need to be tailored to specific groups. In this study, health outcomes were analysed by socio-demographic groups (sex, age at onset, ethnicity and deprivation), cancer type and previous mental health history.

Maintaining service engagement by attending scheduled outpatient appointments is a major aim for transitional health care. However, there is a lack of evidence suggesting that appointment attendance during and after the transitional care period improves health outcomes, particularly in the long-term (8). This study examined whether non-attendance at outpatient appointments increased the risk of negative health outcomes. If appointment attendance affected health outcomes, this would provide evidence for clinicians and policy makers in deciding whether interventions should be focused on trying to increase appointment attendance to reduce negative health outcomes.

One reason for the lack of rigorous data analysis to assess the needs of transitional health care is due to the lack in availability of datasets with extensive follow-up time collected specifically to investigate transition outcomes. To overcome this, historic routine health datasets can be used to provide a novel approach to overcome the paucity of research in this area, particularly for long-term outcomes. In this study, population-based disease registry data from CYA cancer and T1D were linked with other routine datasets (death registration data and hospital admissions data) to assess health outcomes during the transitional care period.

1.3 Childhood and young adult (CYA) cancer and type 1 diabetes (T1D) epidemiology.

Cancer and T1D are two diseases with major differences in treatment and service provision during the transitional care period. Examining two contrasting LTCs provides the opportunity to compare differences and similarities during the transitional care period and between health outcomes.

1.3.1 Childhood and young adult (CYA) cancer.

Childhood cancers (diagnosed in under 15-year olds) and cancers diagnosed in AYAs (between 15 to 24 years) are distinct from adult cancers but also from each other. Both age groups, for example, have their own cancer classification system (see Appendix A) (22,23) due to the need to classify the morphological features of young people’s tumours.

Incidence of cancer in children has increased internationally since the 1980s. This is partly due to better methods for diagnosis (24). Leukaemia accounts for a third of all childhood cancers, with 57% of cases in England diagnosed in under 5s (25). In England, incidence of cancer in AYAs (1,970 new cases in 2014; incidence rate of 276 per million in 2011-2013) is higher than childhood cancer (1,412 new cases in 2014; incident rate of 152.9 per million in 2011-2013), with most cases diagnosed in the 20 to 24 age group (1,261 cases in 2014) (26). Lymphomas are the most common cancer in AYAs for both sexes. However, most female AYA cancers are carcinomas (including cervix and ovary cancer) and most male AYA cancer are germ cell tumours (including testicular tumours). These sex differences are not as apparent in childhood cancers (27).

Cancer treatment is disruptive to daily life and usually consists of one or more therapies including surgery, radiotherapy, chemotherapy and immunotherapy. Once treatment ceases, the patient is labelled as a 'survivor', implying that they have overcome their illness. Some survivors incorporate this into their identity, whilst others view cancer as 'a thing of the past', particularly those diagnosed before 5 years old who may have no memory of treatment (28). This can be problematic for service engagement for follow-up care. Although a daily medical routine is not usually necessary (29), follow-up care is needed to prevent and manage late effects (LEs) right into adulthood (30). Many LEs are a consequence of cancer therapies and can depend on the type and intensity of the treatment (31). Around 74% of childhood cancer survivors will develop an LE such as cardiovascular disease (CVD), recurrent and/or subsequent cancer, endocrine diseases and neurocognitive deficits (32) with a third developing a severe or life-threatening condition (33).

1.3.2 Type 1 diabetes (T1D).

The incidence of T1D is higher in childhood (2,873 cases and incidence rate of 26.5 per 100,000 in 2014-15 in under 16s in England and Wales) than in AYAs, peaking in the 10 to 14 year old age group (34,35). Unlike cancer, at present, there is no sub-categorisation of T1D at diagnosis. T1D is a homogenous disease where daily insulin administration is the standard treatment for all patients and continues into adulthood. The Diabetes Control and Complications Trial (DCCT) was a seminal study, showing that intensive insulin therapy (three or more injections) greatly reduced negative health outcomes in individuals with T1D (36). However, the treatment can be burdensome and difficult to manage. Insulin is either administered through multiple daily injections (MDI) or via continuous subcutaneous insulin infusion (CSII) therapy to maintain blood

glucose levels. Poor glycaemic control can lead to life-threatening acute complications such as severe hypoglycaemia where insulin levels become too high or DKA where there is not enough insulin in the body. In the long-term, poor T1D management can increase the risk of developing chronic microvascular (damage to small blood vessels) and macrovascular (damage to large blood vessels) complications (37). As blood vessels are present throughout the body, this can affect various organs, such as the eyes, kidneys and brain.

CSII therapy is recommended by the National Institute for Health and Care Excellence (NICE) if a patient cannot maintain their HbA1c (glycated haemoglobin which measures average blood glucose for the last two to three months) target with MDI as it delivers insulin continuously and more precisely (38). CSII therapy provides added automation in insulin delivery compared with MDI. It involves the permanent attachment of a programmable pump device to deliver a basal rate of insulin throughout the day and bolus insulin during meal times (38). Although CSII therapy can offer more practical benefits compared with MDI, issues still arise with self-management of T1D during the transitional care period. Wearing a permanent device can be burdensome and can lead to a negative psychological association with the treatment (39,40) and limited clinical success. There is little published research on individuals with poorer clinical outcomes during CSII therapy and whether certain patient groups are more likely to discontinue CSII therapy during the transitional care period. This study compared health outcomes (i.e. HbA1c level as an indicator of T1D control and hospitalisation rate) between individuals who continued and those who discontinued CSII therapy, by socio-demographic groups. This provided evidence for health professionals and policy makers in determining whether discontinuing CSII therapy leads to an increased risk of negative health outcomes and whether certain groups of individuals need to be targeted for specific interventions during the transitional care period.

1.4 Aims, objectives and hypotheses.

The overall aim of this thesis was to use routine health data to assess health outcomes from the transitional care period (15 to 29 years) for individuals diagnosed with an LTC (cancer or T1D) in childhood (under 15 years) or young adulthood (15 to 29 years). Health outcomes included mortality for the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort and HbA1c levels and hospitalisations for the Leeds Children and Young People's Diabetes Service (LCYPDS) cohort and hospitalisations (i.e. inpatient

admissions, accident and emergency (A&E) and mental health attendances and outpatient appointments) for the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) cohort.

It was hypothesised that there would be an increase in negative health outcomes during the transitional care period compared with before and after. This hypothesis was assessed using analysis of linked routine datasets. An increase in negative health outcomes during the transitional care period for contrasting diseases (T1D and CYA cancer) would provide evidence of the need for specialist transition services across diseases. Analysis by socio-demographic (age, sex, ethnicity, deprivation) and clinical characteristics (cancer type, complication type, appointment attendance) would determine whether there is a need for further targeted interventions for specific groups of individuals.

To achieve the overall aim, the following objectives were identified:

1. Compare differences in health outcomes between different age groups before, during and after the transitional care period.

This objective assessed whether the transitional care period was associated with an increase in negative health outcomes compared with younger and older age groups. An increase in negative health outcomes in the transitional care period would support the need for transitional health care.

2. Compare health outcomes between individuals diagnosed with an LTC before and during the transitional care period.

This objective assessed whether there were any differences in health outcomes depending on whether LTC onset occurs before or during the transitional care period. Any differences found between onset groups would indicate the need to consider age at LTC onset in transitional health care policy and practice.

3. Compare health outcomes by socio-demographic groups (sex, ethnicity and deprivation).

This objective assessed whether some socio-demographic groups have worse health outcomes compared to other groups. If any differences were found, this would provide evidence for the need of targeted care directed towards certain socio-demographic groups.

The following objective was specific to the YSRCCYP cohort:

4. Compare health outcomes by cancer type.

Due to the heterogeneity of CYA cancer types, health outcomes may differ between cancer types. This would provide evidence for the need of any cancer specific support.

5. Compare health outcomes by hospital outpatient appointment attendance.

This objective assessed whether attending outpatient appointments were associated with rates of inpatient admission, A&E or mental health attendance. If higher rates of appointment attendance were associated with lower hospitalisations, this would provide evidence for the importance of appointment attendance in reducing negative health outcomes.

6. Compare health outcomes by mental health history.

This objective assessed whether attending with a previous history of a mental health admission was associated with outpatient appointment attendance rates, inpatient admission rates and A&E attendances. If a higher hospitalisation rate or higher rate of non-attendance to outpatient appointments was found, this would indicate a need for specific support targeted at those with mental health issues.

The following objective was specific to the LCYPDS cohort:

7. Assess whether CSII therapy improves health outcomes.

This objective assessed whether CSII therapy could improve health outcomes, particularly within the transitional care period. Analysis included comparisons between individuals who continued and those who discontinued CSII therapy whilst attending the LCYPDS. Health outcomes were assessed by CSII duration to determine whether any improvements were sustained.

1.5 Outline of this thesis.

The literature review in Chapter 2 includes three sections; a review of the concepts and issues around transition, health outcomes in T1D and health outcomes in CYA cancer.

Chapter 3 describes the routine datasets that have been used in this analysis. It describes the source of the datasets, data linkage methodology and the cleaning rules to produce the final datasets. Methodology and statistical analyses used in each dataset are described separately in Chapter 4, Chapter 5 and Chapter 6.

Chapter 4 includes the results of data analysis from the YRDCYP cohort linked to mortality data.

Chapter 5 includes the results of data analysis from the LCYPDS cohort who started CSII therapy.

Chapter 6 describes results from analysis on CYA cancer hospitalisation and mental health outcomes in the YSRCCYP cohort.

Chapter 7 discusses the results from chapter 4 to 6 in detail, including the implications of the study and how this will direct future research in the topic of transitional health care.

Chapter 2 Literature review.

This chapter provides a description of current practices and experiences of transitioning between paediatric and adult services and assessed whether potential factors during this process may influence short-term and long-term health outcomes. This involved reviewing studies from a variety of LTCs to assess common generalised issues surrounding transition. If an increase in negative health outcomes were to be found during the transitional care period, this section of the literature review would have assessed some of the reasons why these increases may have occurred.

This chapter also identified short-term and long-term negative health outcomes associated with T1D and CYA cancer. For CYA cancer, only studies on LEs after the remission period were reviewed. The purpose of reviewing these negative health outcomes was to determine what routine datasets were needed for this study and which health outcomes were important to assess during analysis.

2.1 Literature search methodology.

EMBASE and Ovid Medline databases were used for three searches covering the topics of transition, outcomes of T1D and CYA cancer. A combination of mapped terms and keywords were used before restricting to full text availability, English language and human only research. Details of the search strategies, exclusion criteria and total of articles included for each topic are found in Appendix B. The relevance and quality of research papers were assessed by using a standardised checklist for qualitative studies (41), case-control studies (42), cohort studies (43) and systematic reviews (44).

2.2 The transition process.

Most studies on the topic of transition focused on a single LTC. These LTCs included epilepsy, inflammatory bowel disease, end stage renal disease, human immunodeficiency virus, sickle cell disease, cerebral palsy, transplant recipients, cystic fibrosis and juvenile idiopathic arthritis, as well as CYA cancer and T1D. Studies on mental health, autism and attention deficit hyperactivity disorder were also included. The majority of these studies included individuals who were diagnosed with an LTC during childhood. There were few studies

which included AYAs who were diagnosed during the transitional care period. All studies either used small scale interview or survey data to describe the experience of transition prior to the transfer event. Few empirical studies compared models or interventions of transition or outcomes of transition. Therefore, this review was based on qualitative or survey research from small samples, so may suffer from selection bias, creating difficulty in generalising these results to the general population.

The period before the transfer event was often referred to as ‘transition preparation’ or ‘transition planning’. Although there is consensus that the transition process should be individualised according to a patient’s needs, there have been attempts to standardise transition preparation by expert working groups to help reduce the variation in the transition experience that is often found between different organisations and specialities (45–47). There are some overlaps in recommendations between groups, although these often refer to a single LTC. The NICE guidelines on transition from paediatric to adult services for England and Wales cover all chronic illnesses and recommend the inclusion of key components in transition planning. These include starting the transition process early, having a named worker to coordinate the transition, involvement from the patient, building independence in the patient and involvement from parents/caregivers (20). Each of these components are discussed below, followed by an examination of how transition has been measured.

2.2.1 Starting the transition process at an early age.

A major theme from interview and survey data for AYAs diagnosed with a LTC during childhood was a desire to start the transition process early and gradually taking more responsibility that was developmentally appropriate (47–49). Opinions on the recommended age ranges for the start of transition varied between studies from 11 to 15 years (46,50,51). In practice, some individuals did not start the transition process until after this age range, with some patients and parents reporting to have not received any transition preparation at all (48,52–54). Few studies suggested a better experience for the patient when the transition process began at a later starting age (55,56). Among Brazilian rheumatology clinicians, 88% who were surveyed said that transition preparation should start from 15 years, with 60% stating 15 to 17 to be the optimal age (57). However, it was not apparent from these studies as to whether ‘transition’ was clearly distinguished from ‘transfer’ or at least there was no defined event to signify the start of transition. In some studies, the first conversation with the paediatric provider around transition has been used as

the starting point of transition (52–54), although there was no mention of a requirement to formally record when these conversations occurred or what content should be included. Eklund and colleagues found that although 75% of a sample of 91 patients with attention deficit hyperactivity disorder had no discussions around transition with professionals, the other 25% had said the discussion was only brief (54). Because of this subjectivity at the beginning of the transition process, this has created difficultly in measuring transition. There are no standardised methodologies to quantify how many individuals have started the transition process, so completing a needs assessment and measuring the quality of transition services cannot be achieved (58).

2.2.2 Involvement from a transition coordinator.

From the patient's perspective, lack of coordination between paediatric and adult services was commonly reported (59–61) and was often a reason reported for disengagement in adult services (48,59–65). To navigate between the paediatric and adult services, a single named worker could be a useful coordinator during the transitional care period between the services (8,20,55,57,66,67). The NICE guidelines recommended a named worked for 6 months before and 6 months after transfer event at a minimum (18). However, there was a lack of evidence to support the view that the presence of a transition coordinator makes a positive contribution to the transition experience. In a study by Jensen and colleagues, a social worker transition coordinator improved satisfaction at a transition clinic for rheumatology diseases, although satisfaction levels were still low at 42% (68). In contrast, a transition coordinator who also provided psychosocial interventions to a group of 27 rheumatology patients had higher levels of psychological wellbeing compared with 23 individuals receiving conventional treatment (69). Access to psychosocial care and mental health services was deemed to be important during the transitional care period in a number of studies (46,60,70–72), although in practice, few individuals had access to these services (57,64).

From a provider perspective, paediatric providers tend to find transition coordinators more useful compared with adult providers (45). Although there was general consensus that both paediatric and adult services were responsible for transition, a cultural norm persists where all transitional work and the success of transition depends on paediatric services (50,63,73–76). Few studies assessed whether the adult service that AYAs transitioned to was adequate or appropriate (57,77–79). Many adult providers reported a lack of training around transitional issues (57,80) and a lack of specialist adult services

for some childhood LTCs, making them feel unprepared to take on AYAs (63,67,81). However, positive moves have been made to improve collaboration between services and to provide better staff training in adult providers on AYA and transition issues (60,73,82,83).

2.2.3 Independence and involvement of patient.

Surveys with health professionals found that the main reasons for deciding when a transfer event took place were due to external factors with no involvement in decision making from the patient. These factors included the patient's age, patient's moving away from home, the need for more resource for new paediatric patients or whether the patient had children of their own (57,59). Without patient involvement in decision making during the transition process, patients reported higher levels of anxiety surrounding transfer, even if they felt too old for paediatric care (48,57,81,84–87).

Including patients in decision making around their care increased feelings of control and reduced anxiety, as well as increasing the level of independence and responsibility to deal with their illness. Professionals agreed that AYAs need to be assessed for a certain number of skills (e.g. gathering knowledge about their illness, self-efficacy, self-advocacy, decision making and problem solving) before deciding whether they can be transferred to adult care (51). Readiness tools have been developed to assess these skills, either by the patient themselves, parents or clinicians. There was no data on the use of readiness tools in the UK as they are not mandatory during the transition process. In the USA, the use of these tools tend to differ between different LTCs, suggesting differences in approaches to transitional care between paediatric providers (88,89).

Due to differing expert opinion as to which skills are most important in adult services, tools lack consistency and standardised criteria to determine readiness (50). In a review of 10 readiness tools, it was found that some tools included knowledge of illness, whilst others focused on self-management. There was also a lack of validation for these tools using more than one study and most were disease specific (90). Another criticism of these tools was that there has been no consideration of weighting for more important skills. For example, Hait and colleagues surveyed adult gastroenterologists in the USA (34% response rate) who scored knowledge about medications, prior medical history and impact of smoking and drugs as more important during transition. Less important skills were attending appointments alone and researching condition outside appointments. However, these assessments are based on opinions with

no evidence to determine which skills lead to better health outcomes after transition (91).

Readiness tools rarely included assessment of emotional readiness or life events (90,92,93). Garvey and colleagues suggest a distinction should be made between ‘preparation’ (practical skills and knowledge) and ‘readiness’ (the emotional and psychosocial) (95), as some patients reported feeling that they did not necessarily need to have all the skills to be ready to transfer to adult care (51,96–98) and that confidence and maturity were more important factors (51,77,99). It can be argued that adults themselves do not always have the required knowledge and skills on which AYAs are assessed on, with a lack of research on preparation or readiness conducted in adult care.

2.2.4 Inclusion of family members.

Parental presence is not usually expected in adult services and parents have experienced exclusion from these services (77,100). Although it is assumed that there would be a correlation between increased independence in AYAs with decreasing involvement from parents, qualitative studies show that even though many AYAs want to be more independent, they still want their parents/caregivers involved in their treatment (47,48,61,70,91,101,102). The role of the parent shifted from supervisory involvement to consultant presence (48,77). Some AYAs described wanting their families present for emotional support and as a backup when they could not remember certain details. For example, cancer survivors who were diagnosed and treated before 2 years had little or no memory of their illness and were more likely to rely on their parents for detailed knowledge of the experience (87). However, balancing parental involvement with increased independence can be a challenge. Annunziato and colleagues found that when more independence was given to adolescent transplant recipients, they showed increased non-adherence to medications. Increased parental monitoring was associated with improved adherence (70). However, no studies were found to assess whether this non-adherence was associated with worse outcomes, particularly in the longer term. It may be that ‘helicopter parenting’, where parents struggle to let go of the primary responsibility of their child’s healthcare can prevent independence and self-management in AYAs (49,57,60,66,103) leading to disengagement during appointments as they assume their parents will retain all the knowledge (61).

2.2.5 Differences in transition between socio-demographic groups.

Stollen and colleagues found that paediatric professionals for sickle cell disease viewed socio-demographic factors as having an influence on the transition experience (104). Evidence for this statement comes from the 2009-10 National Survey of Children with Special Health Care Needs (NS-CSHCN) in the USA where transition preparation was more likely to occur in older children and females compared with younger children and males. The most important factor in whether transition preparation occurred was the ability for parents to communicate with health professionals to increase their medical knowledge (8,105,106). Patient knowledge was associated with income levels for 19 to 32-year old cancer survivors who attended a transition clinic in the USA. Those with an income from $10,000 to $24,999 had less knowledge of their diagnosis than any other income group, including the under $9999 group where 74% were students (107). Despite these reported differences in knowledge, no association has been found between socio-demographic groups in readiness for transfer (52).

Cheak-Zamora and colleagues found that 21% of individuals with autistic spectrum disorder (ASD) from the 2005-06 NS-CSHCN received transition preparation, compared with 43% of non-ASD individuals. Only 45% of ASD individuals were encouraged to take more responsibility for their health care compared with 74% of non-ASD individuals (108). This suggests that the type of LTC may also influence the experience of transition preparation (109).

There was only one study that evaluated the difference between those who were diagnosed before and during the transitional care period. AYAs with inflammatory bowel disease who transitioned from paediatric to adult services had lower non-adherence rates to medications (13.2%) than those who were diagnosed and treated in adult services only (24.4%), although the difference was not significant (110).

2.2.6 Measuring successful transition.

With no standardised definition of the starting event for the transition process, the end point of transition is also unclear (51). This means that just as there is no method for measuring transition preparation, there is also no consensus of measuring the success of transition (8,111). Some studies have attempted to define successful transition by appointment attendances in adult services, varying from one clinic visit within 3 months or up to 1 year after transfer (52,112–114). Besides the financial cost, the effect of missed appointments is

not well known, including whether there is an implication for increased A&E attendance and complications. However, non-attendance does not necessarily mean non-adherence. Successful self-management may mean that appointments are only attended for treatment issues. Koshy and colleagues examined the transition period and outcomes in 115 patients with renal transplants in Canada and found that although there was less hospital contact after transition, there was no increased risk of allograft loss. Therefore, attendance only cannot fully assess the degree of successful transition (116).

The problem with using appointment attendance and biomedical outcomes as measures of successful transition is that they do not consider the multidisciplinary nature of transition (117). In a Dutch survey of 433 young adults (18 to 25 years) diagnosed with an LTC, five indicators were used to assess successful transition, including whether the patient was lost to follow-up, the number of missed appointments 3 years after transfer, quality of relationship was with adult provider, self-management and family satisfaction (118).

2.2.7 Overview of the transition process.

Qualitative evidence on the transition process provided examples of where discrepancies appear between clinical recommendations and current practice, such as starting the transition process at a later age, having no access to a transition coordinator, having no direct involvement of patients in decision making regarding the timing of the transfer event and no choice in involving parents/caregivers at appointments after transfer. These discrepancies were reported to have contributed to a negative experience of transition. Although NICE recommendations were aimed to bring standardisation of transitional health care across services in England and Wales, there is still a lack of consensus in definitions of key concepts, particularly the start and end points of the transition process. This imprecision makes it difficult to quantify whether these discrepancies are associated with health outcomes. Quantitative analysis of survey data has provided some assessment of differences between socio-demographic groups in whether transitional care was received. However, this was not applied to the assessment of health outcomes.

2.3 Health outcomes of type 1 diabetes (T1D).

2.3.1 Acute complications.

The two most common types of T1D acute complications requiring hospitalisation are DKA and severe hypoglycaemia, with both complications due to poor treatment management. DKA occurs from deficient insulin levels resulting in high blood glucose levels, whilst severe hypoglycaemia occurs when blood glucose is low, which can be a consequence of too much insulin (119–122). In a Scottish register of all individuals with T1D, a j-shaped association was found between HbA1c levels (glycated haemoglobin which measures average blood glucose for the last two to three months) with the odds of a hospital admission, particularly DKA admissions with higher HbA1c levels. There was no increased admissions at low HbA1c levels due to severe hypoglycaemia (123). This supported the trend in other studies where hospitalisation rates for DKA were higher than for severe hypoglycaemia (124,125). For example, in England and Wales, 5% and 2.3% of children with T1D were admitted to hospital with DKA or severe hypoglycaemia, respectively (126). However, this did not include cases of severe hypoglycaemia where assistance was required from ambulance treatment, without a hospital admission. In a study of 10 NHS Diabetes centres in England and Wales, 71% of self-reported cases of severe hypoglycaemia over a 2-year period were attended to by ambulatory care with only 21% of these cases admitted to hospital (127). This suggests that not all cases of severe hypoglycaemia were being captured by hospital admissions data only, creating an underestimation of severe hypoglycaemia rates (123).

CSII therapy has shown success in reducing HbA1c levels (128–136). However, there were mixed results as to whether CSII therapy can also decrease hospitalisations due to acute complications. Studies examining HbA1c levels in CSII therapy commonly used t-tests or ANOVAs to assess mean HbA1c before and after CSII initiation. These statistical methods are problematic as they do not account for repeated data within the same individuals, thus violating the assumption of independence between observations and resulting in flawed conclusions (137). To overcome this issue, multi-level modelling was used to account for repeated measures when analysing data from a previous study of the LCYPDS cohort. An overall reduction in mean HbA1c of 6mmol/mol (95% CI 3 to 9mmol/mol) (0.5% (95% CI 0.3 to 0. 8%)) was found after one year of starting CSII therapy. There was also a reduction of hospital admissions incidence due to severe hypoglycaemia from 8.9 to 2.4 per 100 person years (138). This supports other studies where mild and severe hypoglycaemia

decreased following the introduction of CSII (130,132,135,139–145). Few studies have found no change in rate of severe hypoglycaemia after starting CSII (136,146).

Studies examining DKA rates with CSII therapy have shown inconsistent results. Some studies have reported lower admissions with CSII therapy (128,134,140,141,145), some have reported no change at all with CSII therapy (136,143,146,147), whilst other studies have reported higher DKA hospitalisation rates with CSII therapy (131,144,148), including the latest National Paediatric Diabetes Audit (NPDA) report (126). This suggests that CSII therapy was beneficial in reducing rates of severe hypoglycaemia, but it was unclear as to whether CSII therapy reduces DKA.

Despite the success of reducing HbA1c levels with CSII therapy, some individuals have reported difficulties in using the CSII device and returning to MDIs (39,40,149). Only one previous study has examined characteristics for individuals who discontinued CSII, where it was found that females were more likely to discontinue (150). There was little published research into the characteristics of individuals with poorer clinical outcomes during CSII therapy.

2.3.2 Chronic complications.

Common microvascular complications include diabetic nephropathy, diabetic retinopathy and neuropathy (151). In the DCCT cohort, it was found that intensive insulin treatment has been effective in reducing these complications by maintaining good HbA1c level and has been shown to reduce the risk of developing retinopathy by 76% and neuropathy by 60% compared with conventional treatment (36,152). After 8 years in the DCCT, despite the control group having similar HbA1c levels than the intensive group, the intensive had less retinopathy. This suggested that starting good HbA1c management as soon as possible after diagnosis contributed to good ‘metabolic memory’. This is where early intensive insulin treatment has a continued effect and can delay retinopathy and slows progression (153). This has great importance in AYAs, where there has been recent evidence that retinopathy and nephropathy (kidneys) complications can start to develop during the transitional care period (154–157).

The DCCT also found that intensive insulin therapy reduced the risk of macrovascular complications, although the risk reduction for CVD was less than half for retinopathy and neuropathy at 30% after a 30 year follow-up (158). In a Scottish T1D registry of individuals over 19 years between 2005 to 2007, the risk of CVD was found to be two to three times greater compared with the

general population and higher in females compared with males (159). CVD events in this study were defined as hospital admissions with International Classification of Diseases (ICD)-9 codes 410–414 and ICD-10 codes I20–I25, so excluded any CVD events recorded under a diabetes-related ICD code, thus possibly providing an underestimation of prevalence in the cohort.

The brain has shown to be particularly susceptible to glycaemic extremes in AYAs during development, where recurrent DKA and severe hypoglycaemia were associated with longer term consequences on brain development (160–162). Neuroimaging has shown some differences between T1D and non-T1D population in the brain with more white matter hyperintensities observed in T1D individuals compared with a non-T1D control group (163). White matter hyperintensities occur due to cerebral microvascular damage and is linked to neurocognitive problems, such as slower information processing, memory and language problems (161,164–166). Despite these neurological issues occurring more in the T1D population, there was no evidence that school performance was different from the non-T1D population (161,167). As school achievement may be associated with quality of life and deprivation levels in adulthood, this was a positive finding. However, these findings were based on small samples, so more research is needed to assess whether these results apply to larger populations.

Although there was no evidence for detrimental academic performance, intensive insulin therapy may affect quality of life due to the negative psychological impact of a burdensome treatment. The rates of depression in T1D were found to be higher compared with the general population (168). Factors within the T1D population that increased the odds of depression included high HbA1c levels and rates of acute complications (149,168–171), being female (149,170), being part of an ethnic minority or having lower income and education achievement level (171).

2.3.3 All-cause and cause-specific mortality.

Despite the success of reducing risk of complications, intensive insulin therapy has only led to a slight reduction in overall mortality risk of 1/1000 patient-years with an additional 6.5 years of intensive insulin treatment during a 27-year follow-up period (172). An excess number of deaths has been found in T1D populations compared with the general population in 17 cohorts in a review of 23 studies from different countries, with the highest standardised mortality rate (SMR) at 8.54 in a Cuban study (173). An overall SMR of 2 (95% CI 1.7 to 2.2) was calculated from 13 European registries, including a subset of the YRDCYP

cohort containing early T1D onset (under 15 years) individuals diagnosed since 1989. The YRDCYP had the second highest SMR of all 13 registries at 4.2 (95% CI 2.2 to 5.6) (174). This was similar to the SMR compared with the general population of England and Wales found in a previous study of the overall YRDCYP cohort including late T1D onset (15 to 29 years) diagnosed from 1978 at 4.7 (95% CI 3.8 to 5.6) (175).

By age at onset, this previous study of the YRDCYP found a non-significantly higher SMR in the late onset group (15 to 29 years) compared with the early onset group (6.2 (95% CI 4.3 to 8.6) vs 4.2 (95% CI 3.2 to 5.5)) (175). Higher risk of mortality in late onset compared with early onset was also found in a Finnish cohort, particularly for deaths due to acute complications of T1D (176). Few population registries have included individuals with late T1D onset in mortality, so research into potential differences between onset groups is sparse. However, studies have shown that death due to acute complications was the leading cause of death for under 30 year olds, whilst CVD was the leading cause of death for older adults (177–183). As with complications, increased risk of death has often been linked with increases in HbA1c (184–187) which are difficult to control in AYAs who have the highest HbA1c levels due to changes in insulin resistance during puberty (188,189). Both the National Diabetes Audit (NDA) and NPDA showed the need for national improvements to raise standards of care for individuals with T1D, as only a third in England and Wales receive all necessary annual care processes, with less than 20% of individuals actually reaching recommended targets for HbA1c, blood pressure and cholesterol (190,191).

The SMR for all-cause mortality was found to be higher in females than males in a number of studies (174,192–196). Studies examining sex differences for cause-specific mortality have shown mixed results with one study showing higher mortality for females in diabetes-related causes of death compared with males (177), whilst in a Norwegian cohort, the risk of death in women from acute complications was half than in women compared with men (182). The DCCT cohort also found that there were nominally more suicides in the intensive treatment group (n=5; 11.6%) compared with the conventional treatment group (n=2; 3.1%), although there were only a total of 7 deaths due to suicide in total, so these results cannot be generalised to population level (172).

Socio-economic status has also been found to affect the risk of mortality, with an increase in risk found in the most deprived group for individuals diagnosed with early T1D onset (186,197–199). Conway also reported a high excess of deaths in the most deprived groups and found that the excess was higher in African Americans compared with white Americans (200), suggesting that

ethnicity may be a more important risk factor for mortality than deprivation. The Allegheny cohort in the USA also found differences in ethnic origin, where excess deaths due to acute complications were found in individuals with black ethnicity (201,202). There were no studies found exploring the association between ethnicity and mortality in the UK.

2.3.4 Summary of type 1 diabetes (T1D) health outcomes.

Maintaining good glycaemic control can be beneficial in preventing and delaying onset of T1D complications, especially when good self-management skills are implemented as early as possible after T1D diagnosis. This means that good HbA1c control during the transitional care period is vital in reducing the risk of negative health outcomes, not just in the short-term but also in the long-term. There was some evidence to suggest that AYAs have issues with self-management, as it was shown that deaths from acute complications are increased at ages during the transitional care period. CSII therapy may be a suitable treatment option for AYAs as it was shown to be effective in reducing HbA1c, although there was less convincing evidence that hospitalisations were reduced. There was also a lack of research on individuals who are most likely to discontinue with CSII therapy and may need additional support.

2.4 Health outcomes of childhood and young adult (CYA) cancer.

Many LEs are due to treatments in children where they are more prone to later issues during organ development (203) and can depend on the type and intensity of the treatment (31). LEs can be categorised by CVD, subsequent cancer, endocrine (including fertility) and neurocognitive (32). Compared with samples from the general population, 5-year childhood cancer survivors were shown to have an excess in hospitalisations. The Childhood Cancer Survivor Study (CCSS) in the USA found a 1.6-fold risk of hospitalisation in survivors (204), whilst in a Dutch cohort the risk was 2.2-fold (205).

2.4.1 Cardiac and Cardiovascular disease (CVD).

Anthracyclines are commonly used in chemotherapy to treat a variety of cancer types, but has shown to have side effects resulting in direct cardiac injury due to the formation of free radicals and cardiotoxic alcohol metabolites. There may

also be an association between cancer therapies with the development of CVD due to an increase in insulin resistance such as lipid abnormalities, adiposity and hypertension (206). Using speckle tracking echocardiography for patients treated with anthracyclines, there was evidence of cardiotoxicity from after a year of treatment (207). Although it was not known whether this had led to future cardiac disease, other studies have shown that high dose heart radiation and anthracycline treatment was associated with risk of cardiac disease congestive heart failure (208–210). Compared with the general population, Kearney and colleagues used echocardiograms at rest and during exercise and found that cancer survivors had comparable left ventricle function with controls during rest but had reduced function compared with controls during exercise. Once a cancer patient gets cardiac dysfunction, the outcome was poor with 50% survival rate after 5 years (208,210). In the British Childhood Cancer Survivor Study (BCCSS) cohort of 34,489 5-year survivors, there were 3.4 times the expected total of cardiac deaths. The BCCSS also found that excess deaths have reduced since the 1980s, coinciding with a reducing of anthracycline levels in cancer treatments (211).

For CVD, a recent systematic review of 63 papers which included individuals diagnosed with cancer at 25 years and under found an average weighted prevalence of 19.7% for hypertension and 2.3% for stroke, although there was a lack of studies in the review which looked at socio-demographic factors or cancer type (212). Previous analysis on the YSRCCYP did find a difference in CVD between age at diagnosis groups, with an excess 3-fold risk of developing CVD for childhood cancer survivors compared with the general population, although no significant excess is CVD was found for those diagnosed during the transitional care period (15 to 29 years) compared with the general population (213). However, for cerebrovascular events (including cerebral haemorrhage, cerebral infarction and subarachnoid haemorrhage), the Teenage and Young Adult Cancer Survivor Study did find a higher excess for those diagnosed during the transitional care period. Of the 178,962 15 to 39-year olds diagnosed with cancer in England and Wales between 1971 and 2006, there was a 40% increased risk of hospitalisation for a cerebrovascular events compared with general population, with the highest risk for those who were diagnosed in the 15 to 19-year age group by 3.6-fold (214).

2.4.2 Subsequent malignant neoplasms.

Subsequent malignant neoplasms are distinct from initial cancer diagnosis. Pooled analysis from four studies showed a radiation dose-related association

with increased risk of developing thyroid cancer in childhood cancer survivors, where the risk remained higher after decades since initial radiation treatment, with or without chemotherapy (215). Although beyond moderate doses of radiation, the risk of thyroid cancer plateaus, possibly due to cell death (216). A reduction in risk developing subsequent cancers in the 1990s was found compared to the 1970s, coinciding with reductions in radiation intensity and dosage in cancer treatment (217).

The BCCSS found that the most common subsequent cancers in 17,981 5-year childhood cancer survivors were central nervous system (CNS) neoplasms, breast cancer, non-melanoma skin cancer, digestive, genitourinary. Those who were initially diagnosed with CNS neoplasms, leukaemias, Hodgkins lymphoma and Wilms tumours had the highest percentages of subsequent cancers (218). This was similar to the CCSS in the USA where individuals initially diagnosed with Hodgkins lymphoma, leukaemia, soft issue, bone and CNS neoplasms had the highest percentages of subsequent cancers. There was a cumulative incidence of 9.3% for a subsequent cancer after 30 years follow-up of initial cancer diagnosis in 14,358 childhood cancer survivors with 5-year survival. Females and young age at initial cancer diagnosis were risk factors for subsequent cancer compared with males and older age group, respectively (219).

2.4.3 Endocrine conditions.

Around 57.6% of childhood cancer survivors have at least one endocrine condition (220). Endocrine conditions due to high dose radiation, chemotherapy exposure and stem cell transplantation include growth deficiency (221), reduced bone health (32,222–224) and fertility issues (225).

In a Dutch cohort of 573 childhood cancer survivors, around 10% of the cohort had a significantly reduced height in adulthood. A radiation dose-related association was found where those who had higher doses of radiotherapy during cancer treatment had significantly shorter height in adulthood, with greatest height loss in individuals who received total body radiation and craniospinal radiation. This could be due to spinal radiation causing skeletal damage in the spinal column and cranial radiation causing damage to the hypothalamo-pituitary axis, which can both lead to growth reductions (226). This theory could be supported by a study of brain tumour survivors, where growth was found to be impaired for a higher percentage of individuals at 60%, which included individuals with a growth hormone deficiency (227).

Fertility issues have been shown to arise when children were treated for cancer during puberty. For females, radiotherapy has been associated with damage and size reductions to both the ovaries and uterus, which can lead to adverse fertility and pregnancy outcomes such as infertility, miscarriage and low birthweight (228–230). Those who received pelvic, spinal or total body radiation were at increased risk of these adverse outcomes due to uterine volume. Individuals who received chemotherapy during cancer treatment were found to be at risk for ovary deficiencies only. Hodgkin lymphoma survivors were found to have the greatest reductions in ovarian reserve compared with individuals diagnosed with leukaemia, sarcoma and other lymphomas (230). Despite these deficiencies, there was no evidence for an increase in adverse pregnancy outcomes compared with the general population (231–233).

Fertility issues were also reported in males survivors. Azoospermia has been reported in 18% of male survivors in a Swedish cohort (225). Almost 80% of males who have conceived were reported to be able to do so naturally (234). These studies are descriptive and there were no studies with comparison to the general population.

2.4.4 Neurocognitive deficits.

Compared with sibling controls, survey data from the Swiss Childhood Cancer Survivor Study reported a higher percentage of childhood cancer survivors who had cognitive deficiencies (20% vs 40%), with highest risk in individuals diagnosed with CNS neoplasms and individuals who received cranial radiation with or without chemotherapy during treatment (235). These cancer treatments increased the risk of damage to neurons and a reduction in progenitor cells in the hippocampus, particularly during brain growth (236). Survivors of paediatric brain tumours were shown to have lower hippocampal, putamen and whole brain volume compared with controls (237). This can create problems with memory and attention (235,237,238). Other reported cognitive deficits included language, mathematics and perceptual motor skills in survivors of CNS neoplasms, acute lymphoblastic leukaemia and non-Hodgkin lymphoma (32,237,239,240).

Exposure to cranial radiation was also associated with increased rates of depression in non-Hodgkin lymphoma survivors (241). However, it was not clear if this was due to deficits in the brain or whether cancer survivors, regardless of diagnosed cancer type, experienced lower quality of life compared with the non-cancer population (238). Recklitis and colleagues found an association between health outcomes and suicide ideation, particularly those with CNS neoplasms

who had more neurocognitive difficulties affecting occupational, educational and social life circumstances (242). A significant association between psychological disorder and quality of life was found in a French study including childhood cancer survivors and controls, with a higher risk of psychological disorder and alcoholism in survivors compared with the general population (243).

Schwartz and Drotar (2006) found that although most childhood cancer survivors had adjusted well into young adulthood (18 to 28 years), childhood cancer survivors were 5 times more likely to develop post-traumatic stress disorder (PTSD) compared with the general population (odds ratio 4.67 95% CI (1.14 to 19.15)) (244). Although PTSD has been linked to post-traumatic growth in other life-changing stressors (e.g. physical assault or terrorist attack), there was weak evidence that this occurred in cancer survivors, possibly due to multiple stressors and no real end-point in trauma (245,246). Cancer diagnosis during adolescence and treatment severity were also found to be possible risk factors for psychosocial issues (247). Good relationships with providers, family and peers have been show to provide great support for AYAs with cancer during the transitional care period (248).

2.4.5 Summary of childhood and young adult (CYA) cancer health outcomes.

LEs are varied in CYA cancer survivors as they depend on the type and intensity of the treatment received during their primary cancer diagnosis. Although the incidence of LEs have been reducing over time due to a decrease in the intensities of treatments, there is still an excess of hospitalisations in survivors compared with the general population. It is important that survivors are monitored after treatment completion, particularly during the transitional care period to detect developmental deficiencies and to provide any additional psychosocial support. Appointment attendance has been used as a measure for successful transition in previous studies from other LTCs. However, these studies have rarely assessed whether appointment attendance was associated with long-term outcomes.

For both T1D and cancer, existing studies have mostly included cohorts with early disease onset diagnosed before 15 years. There were few studies which compared health outcomes between individuals diagnosed before and during the transitional care period. There has also been a lack of assessment between socio-demographic groups, particularly for ethnicity and deprivation.

2.5 Chapter summary.

This chapter summarises current experience and practice of transitional care across multiple LTCs and explored the difficulties in achieving standardisation of care which may affect the risk of negative health outcomes. These negative health outcomes for T1D and CYA cancer were also assessed to help determine which routine datasets were to be used for analysis. Descriptions of these routine datasets, alongside data linkage and data cleaning methodology before data analysis are described in Chapter 3.

Chapter 3 Routine datasets.

The registry data analysed in this study were the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) and the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP). These were population-based registers for individuals diagnosed with T1D (YRDCYP) and cancer (YSRCCYP) before 30 years of age (249,250). Both these registers had data collected over at least a 35-year period, providing a lengthy follow-up time to assess long-term health outcomes. These datasets were linked to other routine datasets for analysis of health outcomes. In addition, data from T1D patients receiving CSII therapy at the Leeds Children and Young People Diabetes Service (LCYPDS) were analysed to assess whether CSII was effective in reducing negative health outcomes in the transitional care period.

Each of the routine datasets used in this study were collected for different purposes. They were compiled over different time periods and geographical coverage, using different sources of information and data collection methodologies. This meant that each dataset had their own unique issues in data cleaning and data linkage. In this chapter, details on data collection, data cleaning and data linkage methodology to other routine datasets are described for each disease cohort. Methodology for statistical analysis for each cohort is presented separately alongside the results in chapters 4, 5, and 6.

3.1 Yorkshire Register of Diabetes in Children and Young People (YRDCYP).

The YRDCYP is a population-based register of all individuals diagnosed with T1D, identified from all specialist diabetes services, hospital admissions with a diabetes discharge and primary care records, within the former Yorkshire Regional Health Authority (YRHA). Data were extracted from clinical notes from these sources to provide diabetes diagnosis (diabetes type and diagnosis date) and demographic information (full name, sex, date of birth, address and postcode of residence at diagnosis) (249–251).

3.1.1 Age at type 1 diabetes (T1D) onset group classification.

The YRDCYP began collecting data retrospectively in 1989 on individuals diagnosed with early T1D onset (diagnosed in children under 15 years) and

treated in the former YRHA from 1978 (Figure 3.1). The region currently has an estimated population of 4 million (7% of the population of England and Wales) (252). From 1991, the YRDCYP extended the data collection criteria to include late T1D onset (diagnosed in young people aged between 15 to 29 years). The YRDCYP currently includes data up to 2013.

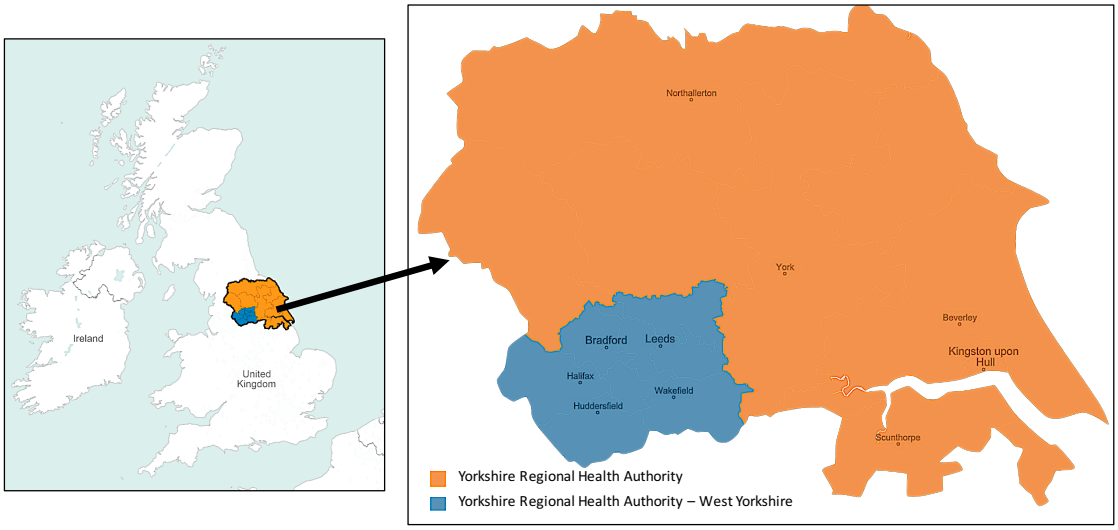


Figure 3.1: Map of the former Yorkshire Regional Health Authority (YRHA).

Due to consent issues, only data on individuals with early T1D onset who were resident in the YRHA at T1D diagnosis, and data on individuals from the late T1D onset group who were resident in West Yorkshire (Bradford, Calderdale, Kirklees, Leeds and Wakefield) at T1D diagnosis since 1991 could be included in the analysis. West Yorkshire comprised of approximately 57% of the total YRHA population (253). Any individuals who were resident outside the designated geographical area were excluded from this study.

3.1.2 Ethnicity classification.

Data on ethnicity were inconsistently recorded on the YRDCYP. Imputation for ethnicity was completed using a software algorithm called Onomap, which calculated probability scores for ethnic categories using full name. Although there were some sensitivity issues for classifying non-British ethnicities, Onomap had the advantage over other ethnicity algorithms by using multiple dimensions of identity (religion, geographic origin, ethnic background and language) for classification and by having a larger coverage of ethnic groups compared with other algorithms (254).

Individuals with incomplete full names could not be used by Onomap and were classified with an unknown ethnicity. Any individuals with names classified by Onomap with an ambiguous origin were also classed with an unknown ethnicity.

3.1.3 Deprivation classification.

Each individual in the YRDCYP cohort was assigned a deprivation score from the Townsend index, according to their ward area (derived from postcode of residence at the time of diagnosis). The Townsend index calculated deprivation using variables from the UK decennial census (unemployment, overcrowded households, car/van ownership, home ownership) (255). Townsend scores and ward areas were calculated from the census year 2001. This census year was chosen as this was approximately midway of the cohort period. Ward areas within the whole YRHA were ordered by Townsend index score and divided into five quantile groups; ‘Most deprived fifth’, ‘2nd most deprived fifth’, ‘3rd most deprived fifth’, ‘2nd least deprived fifth’ and ‘Least deprived fifth’.

Individuals in the early T1D onset group were assigned to a deprivation group based on geocoding the former YRHA ward area of their place of residence at diagnosis. West Yorkshire included many of the most deprived wards in the former YRHA, so geocoding ward area for individuals in the late onset group using the same geocoding as the early onset group would inflate the most deprived totals. Therefore, ward areas within West Yorkshire only were also ordered and split into the five quantile groups, so the late T1D onset group could use geocoding from West Yorkshire only.

The Index of Multiple Deprivation was also considered for assigning deprivation groups. This calculated deprivation by output area instead of ward code. Output areas were approximately equal in population size, so there would have been more of an equal spread across deprivation categories. However, the Townsend index was preferred due to its focus on material deprivation.

3.1.4 Data cleaning.

The YRDCYP dataset was stored in a Structured Query Language (SQL) database across multiple tables (Table 3.1).

Table 3.1: Structured Query Language (SQL) table descriptions of the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) database.

SQL table name	SQL table description
dbo.patient	Identifiable data including full name, sex, date of birth and ethnicity (if recorded). Linked to dbo.diagnosis and dbo.patient_addresses by the individual identifier p_id.
dbo.diagnosis	Diagnosis data including diagnosis date, diabetes type. Linked to dbo.patient by the individual idenitifer p_id. Linked to dbo.patient_addresses by the individual identifier p_id and also the diagnosis identifier d_id.
dbo.patient_addresses	Residential address of the patient at T1D diagnosis.

These tables were joined by a SQL query via an individual identifier (p_id) available in all tables and a diagnosis identifier (d_id) found in the dbo.diagnosis and dbo.patient_addresses tables. Within the SQL query, the data were cleaned to provide the final YRDCYP cohort.

All individuals with a diagnosis of T1D on the YRDCYP were included in the analysis, except in the following circumstances:

- Individuals diagnosed with more than one diabetes type if T1D was not recorded at the latest diagnosis date. Any diabetes type diagnosis occurring before the latest date of diagnosis was assumed to be incorrect.
- Individuals diagnosed with T1D as a secondary condition (e.g. secondary to cystic fibrosis). These types of diabetes have different characteristics from primary T1D.
- Individuals with a T1D diagnosis within 6 months from birth as they should have been classified with neonatal diabetes instead of T1D.
- Individuals with missing residential address at date of diagnosis as it could not be determined whether the individual was resident in the YRHA area for early onset individuals or in West Yorkshire for late onset individuals.

- Individuals with late T1D onset who were diagnosed before 1991 due to consent issues.
- Individuals with missing/incomplete demographic or clinical data essential for analysis:
    - One person with missing date of birth was excluded from the cohort as it could not be determined whether this person had early or late onset T1D.
    - Two individuals had no recorded date of diagnosis. Of these two individuals, one person did have a diagnosis age recorded so date of diagnosis was imputed using diagnosis age and date of birth. There was no information available for the other individual to impute date of diagnosis, therefore, this individual was deleted from the cohort.
    - Five individuals from the early onset group had missing sex data. Sex was imputed by examining the first name of four of these individuals. The remaining person had a first name which could be classed as male or female and was left with an unknown sex code.
    - After data linkage to the Office for National Statistics (ONS) death certification data (described in section 3.1.5), one person was deleted from the cohort as they were reported on the ONS death dataset with missing date of death and underlying cause of death. Both these fields were essential for analysis.

The stages of data cleaning are summarised in Figure 3.2.

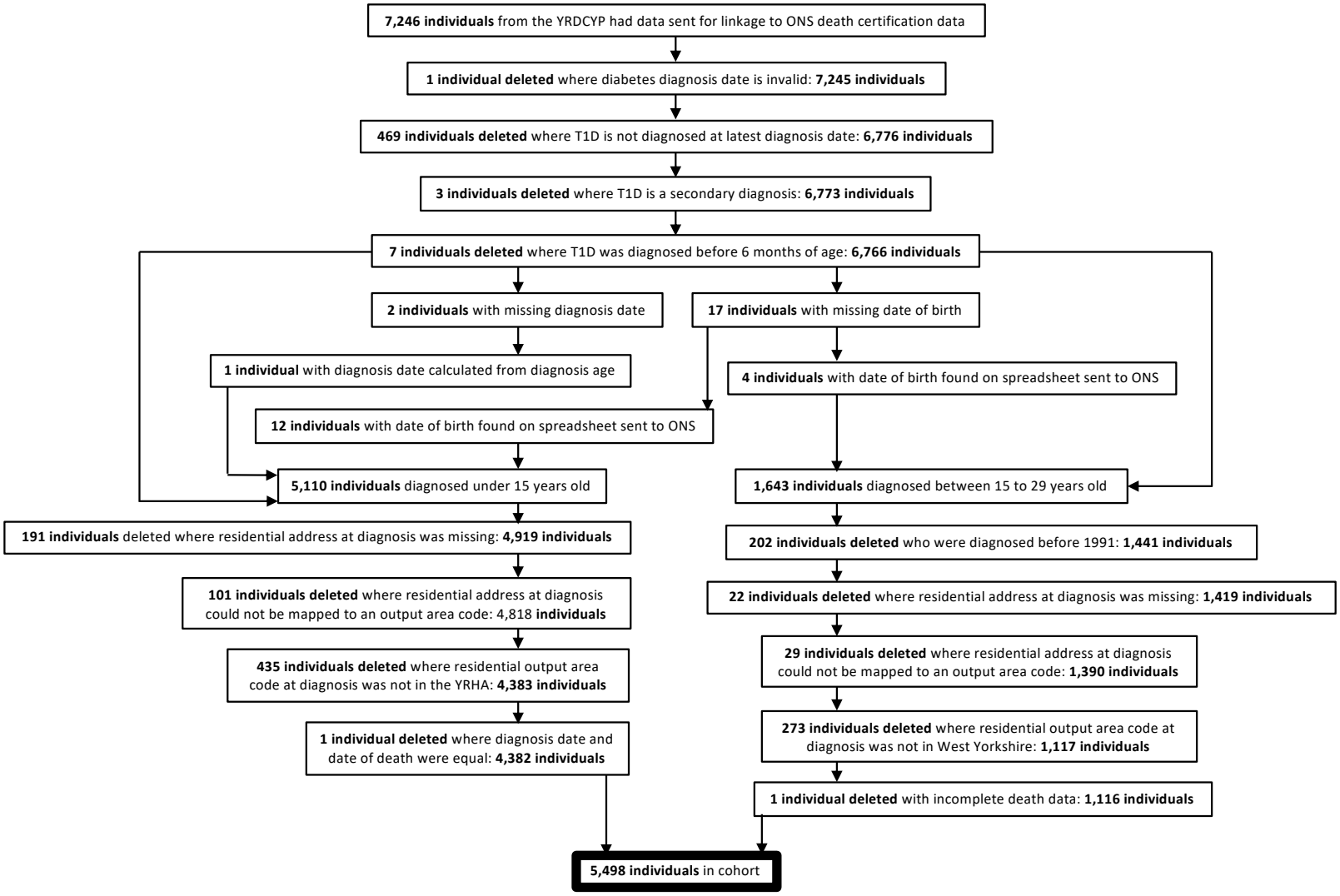


Figure 3.2: Data cleaning for Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort.

3.1.5 Data linkage to death certification data from the Office for National Statistics (ONS).

Personal identifiable data (NHS number, date of birth and name) from the YRDCYP were previously sent to the ONS for data linkage to death certification data. The data from the ONS included details from the original death certificates such as place and date of death, as well as any free text. This free text was used by the ONS to create a number of coded cause of death variables and a single underlying cause of death variable, using the ICD-10 coding system. Underlying cause of death was defined as "the disease or injury which initiated the train of morbid events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury" (252, p.31).

As the coding for underlying cause of death at ONS was not clinically validated, this variable was assessed by a specialist clinician. This involved assessing all the free text from the ONS dataset to determine whether the current underlying cause of death code was correct. If an individual was assessed as having an inaccurate code, a new ICD-10 was used assigned to the underlying cause of death variable.

Death certification data were received by ONS in csv format, with death information on the YRDCYP up to 31st December 2015 (Figure 3.3). These were uploaded onto the SQL database as a view. Data from this view were joined to the YRDCYP SQL tables to create a final dataset extracted on 26/11/2016 for analysis in STATA (257).

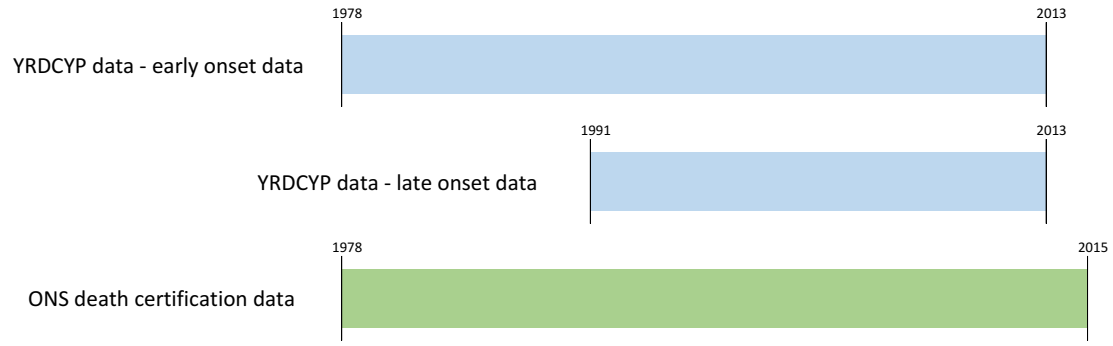


Figure 3.3: Timeline for Yorkshire Register of Diabetes in Children and Young People (YRDCYP) and Office for National Statistics (ONS) death certification datasets.

3.2 Leeds Children and Young People's Diabetes Service (LCYPDS).

The LCYPDS delivers care to under 19-year olds newly diagnosed with diabetes. The service offers CSII therapy to patients in accordance with NICE guidelines. Administrative data were extracted for T1D patients attending the LCYPDS who had started CSII therapy between 2002 and 2013.

The dataset included clinical data on diabetes diagnosis date, CSII start date (and CSII end date for any individuals who discontinued CSII therapy) and HbA1c values at each appointment attended at the LCYPDS up to 2015. Data on any recorded hospitalisations (hospital inpatient admission or A&E attendance) whilst attending the LCYPDS were also included. Demographic data included age and sex. Deprivation and ethnicity could not be included due to missing data.

3.2.1 Data cleaning.

There was a previous STATA dta file containing data on the LCYPDS for individuals attending the service on CSII therapy from 2002 to the end of October 2007. These data had already been cleaned and analysed.

A list of individuals attending the LCYPDS up to 2013 was obtained from the lead clinician. This list had been verified by the lead clinician as having correct and up to date demographic and clinical data. Health professionals at the LCYPDS enter their patient data into a Microsoft Access database. The Access database included clinical and demographic data across a number of tables. A copy of the database, updated up to April 2016, was made available to extract data for the listed individuals. Table 3.2 includes the Access tables and their descriptions for the extracted data.

Table 3.2: Microsoft Access database tables for the Leeds Children and Young People's Diabetes Service (LCYPDS).

Access table name	Access table description
Patient	Identifiable data including full name, sex, date of birth, ethnicity (if recorded) and CSII start date. CSII date was also collected if the individual discontinued CSII therapy during attendance to the LCYPDS.
ClinicalBaselineData	Clinical data (including HbA1c measurements) collected from type 1 diabetes diagnosis date and before the recorded CSII start date.
ClinicalData	Clinical data (including HbA1c measurements) collected on and after the recorded CSII start date but before any recorded CSII end date.
ClinicalDataqPostCSIITherapyAnnualReview	Clinical data (including HbA1c measurements) collected on and after the recorded CSII end date.
Hospital Admissions	Any recorded inpatient admission or A&E attendance during attendance at the LCYPDS.

These tables were extracted from Access into multiple sheets in an Excel file. From these multiple datasheets, a single table was created and included a new variable to determine whether an appointment occurred before, during or after CSII therapy.

The Excel file was exported into STATA, where it was formatted and joined to the old dataset. For individuals with data in both new and old datasets, it was found that the old data had been duplicated in the new dataset and included more recent information. Therefore, data from the new dataset were used for these individuals.

The stages of data cleaning are summarised in Figure 3.4. All individuals with a diagnosis of T1D were included in analysis, except in the following circumstances:

- Individuals diagnosed with more than one diabetes type if T1D was not recorded at the latest diagnosis date. Any diabetes type diagnosis made before the latest date of diagnosis was assumed to be incorrect.
- Individuals diagnosed with T1D as a secondary condition (e.g. secondary to cystic fibrosis), as these types of diabetes have different characteristics from primary T1D.
- Individuals with a T1D diagnosis within 6 months from birth as they should have been classified with neonatal diabetes instead of T1D.
- Individuals who did not have HbA1c values recorded both before and after the CSII start date as both pre- and during-CSII HbA1c values were needed to examine HbA1c change with CSII therapy.

Records for individuals were deleted in the following circumstances:

- 18 records were deleted as the date of the clinical record was invalid (i.e. year was recorded as 1900).
- Any hospitalisation recorded before the T1D diagnosis date was deleted.
- Any clinical records where date of clinical record was after CSII end were only included in analysis for comparisons between individuals who continued and discontinued CSII.

There were seven individuals where sex code was derived using first names.

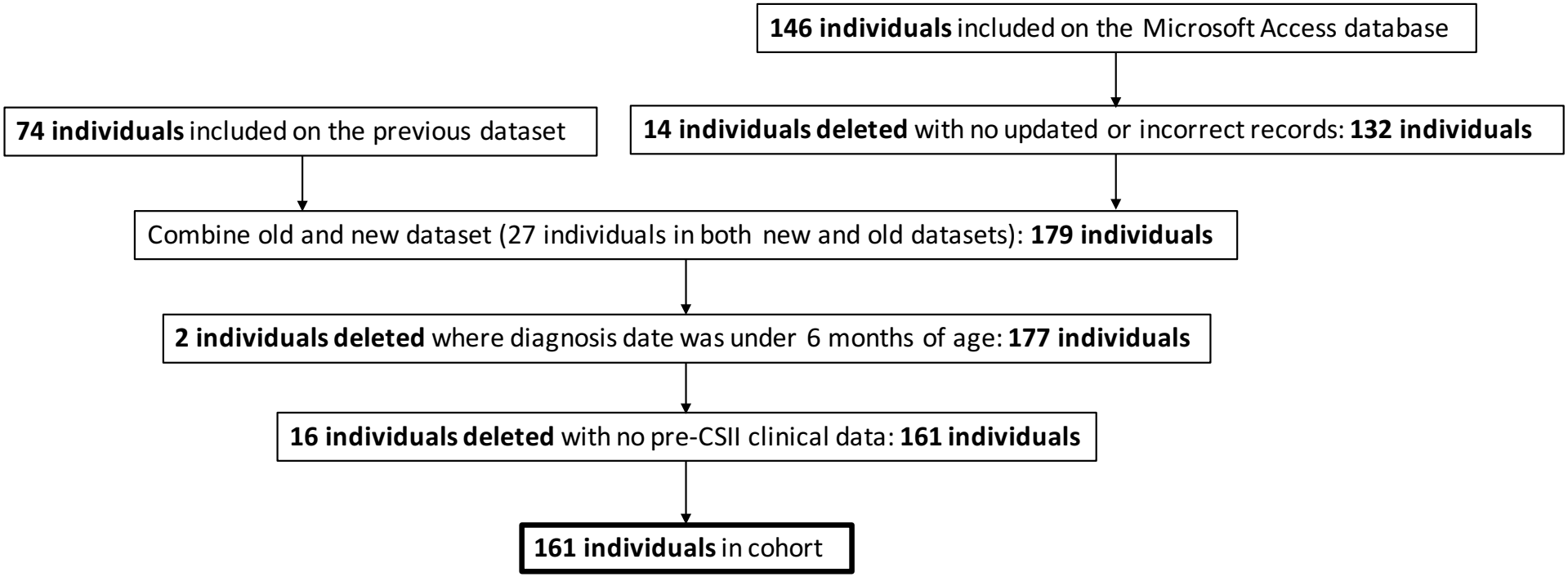


Figure 3.4: Data cleaning for Leeds Children and Young People's Diabetes Service (LCYPDS) cohort.

3.2.2 Defining the pre-, during and after continuous subcutaneous insulin infusion (CSII) time periods.

HbA1c values and hospitalisations were categorised as occurring pre-CSII, during CSII or after CSII therapy (for individuals who discontinued CSII therapy only) (Figure 3.5).

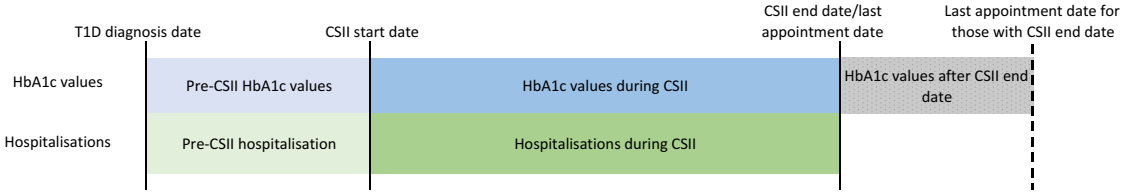


Figure 3.5: Timeline for pre-, during and after continuous subcutaneous insulin infusion (CSII) time periods.

Pre-CSII therapy included the period from the T1D diagnosis date to the day before the CSII therapy start date.

During CSII therapy included the period from the CSII start date. CSII duration ended on the last recorded appointment date if there was no CSII end date. If a CSII end date was recorded, CSII duration ended on the day before a recorded CSII end date.

For individuals who discontinued CSII therapy, the CSII end date marked the beginning of the after CSII period.

There was one person who ended CSII therapy but then started again around 4 years after. This person was counted twice. Each CSII period for this person was calculated using the following method (Figure 3.6):

- The mid-point between ending CSII and starting CSII for the second time was calculated.
- Dates from the day after the CSII end date to the day before the mid-point were classed as after CSII end.
- Dates from the day of the mid-point to the start of the second CSII start date were classed as pre-CSII for the second CSII period.

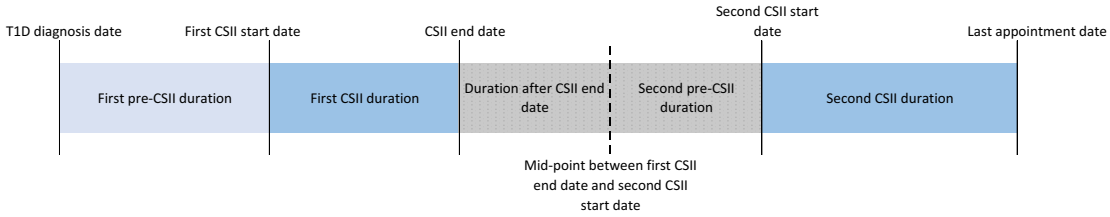


Figure 3.6: Pre-, during and after continuous subcutaneous insulin infusion (CSII) duration with more than one CSII therapy periods.

3.3 Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP).

The YSRCCYP is a population-based register of all individuals under the age of 15 who were diagnosed with childhood cancer from 1974 in the former YRHA. From 1990, data on individuals diagnosed with late cancer onset (aged between 15 and 29 years) were also collected. The tertiary referral paediatric oncology centre at Leeds General Infirmary and the Northern and Yorkshire Cancer Registry and Information Service are the main sources for the YSRCCYP. Records are annually cross-checked with the National Cancer Registration Service. As an ongoing register where data are updated regularly, the number of people within the cohort depends on when an extract of the data is taken. In this analysis, a cohort from the register was taken on 7th February 2017.

The data from the YSRCCYP included sex, date of birth, date of cancer diagnosis and cancer type and residential address at the time of cancer diagnosis. Date of death information from Public Health England was also included in the YSRCCYP extract. Any individuals with a date of death within the first five years after their first recorded cancer diagnosis were excluded from this analysis.

3.3.1 Cancer type classification.

The cancer type at diagnosis was defined from the YSRCCYP data from the first recorded diagnosis date. This field classified cancer types by the 12 major diagnostic groups described by the International Classification of Childhood Cancer-3 (ICCC-3) for both early and late cancer onset groups.

The YSRCCYP data extract included 259 individuals where their tumour could not be classified under the ICCC-3. These individuals were excluded from this analysis as their tumours were identified as having a benign histology.

If an individual was diagnosed with more than one cancer type on different dates, the cancer type diagnosed on the earliest date was assigned to the individual. No individuals had more than one cancer type on the same date on the earliest cancer diagnosis date.

3.3.2 Ethnicity classification.

As with the YRDCYP, ethnicity was inconsistently recorded on the YSRCCYP. Therefore, imputation for ethnicity was also completed using Onomap. However, the Onomap software was used to assign ethnicity on the YSRCCYP cohort from an extract taken on 06/07/2016 (before the extraction date in this analysis) with 9,001 people. Therefore, ethnicity could not be assigned to all individuals in the cohort. The Onomap software could not be run on the current extract due to licencing issues of the software.

3.3.3 Deprivation classification.

As with the YRDCYP cohort, the Townsend index was used to determine deprivation group. This used the same methodology as for the YRDCYP (section 3.1.2) of using residential address at time of diagnosis.

3.3.4 Duplicate records and exclusions in the YSRCCYP dataset.

Data extracted from the register on 07/02/2017 included 9,470 people with 9,885 records. There were duplicate records for 148 people for the following reasons:

- 18 people were recorded with more than one cancer diagnosis of the same cancer type on the same day. These duplicate records were deleted.
- 123 people had two cancer diagnoses of different cancer types on different days. The first cancer diagnosis was included and the second diagnosis was deleted.
- 7 people had three cancer diagnoses of different cancer types on different days. The first cancer diagnosis was included and the second and third diagnoses were deleted.

In addition, 2,232 people were excluded from the analysis as they had a date of death within the first 5 years after initial cancer diagnosis. Therefore, the total individuals in the cohort was 7,238.

3.3.5 Hospital Episodes Statistics (HES) datasets and the Mental Health Minimum Data set (MHMDS).

The YSRCCYP cohort was linked to Hospital Episode Statistics (HES), which included data on outpatient appointments and hospital inpatient admissions and accident and emergency (A&E) attendances recorded in any secondary care NHS hospitals in England. In addition, the YSRCCYP was also linked to the Mental Health Minimum Data set (MHMDS) which included data on admissions to secondary mental health services.

These datasets provided assessment of whether attendance to follow-up outpatient appointments reduced complications. Data on inpatient admissions, A&E attendances and mental health admissions were used as proxy measures for complications. If a reduction in hospitalisations was found, this would indicate the importance of increasing attendance to follow-up outpatient appointments in reducing complications.

HES data for the YSRCCYP cohort had previously been requested from NHS Digital (formerly the Health and Social Care Information Centre). This involved sending YSRCCYP data to NHS Digital where this could be linked to HES data via personal identifiable data (NHS number, date of birth, sex and postcode at cancer diagnosis). The YSRCCYP identifier field was also sent to NHS Digital and was included in the final linked HES dataset.

The linked HES data received from NHS Digital included separate datasets on inpatient admissions, outpatient appointments and A&E attendances, as well as data from the MHMDS.

The different datasets covered different time periods between 1997 to 2017. This was due to the availability of the HES datasets and the different timings of when each dataset was requested. Figure 3.7 illustrates the time coverage of the different datasets in comparison with the YSRCCYP data.

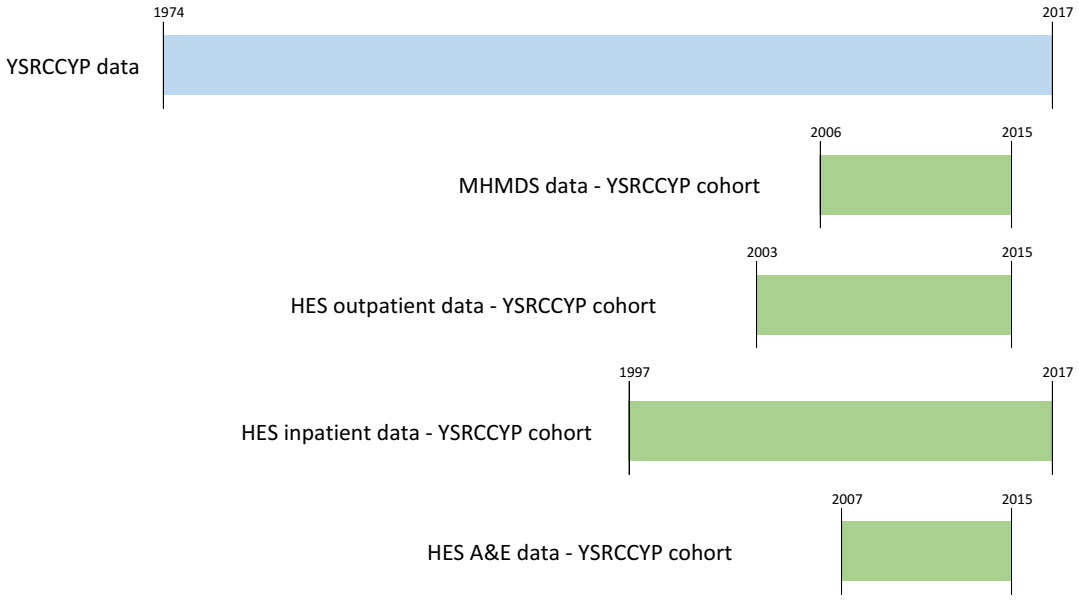


Figure 3.7: Timeline for Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP), Hospital Episode Statistics (HES) and Mental Health Minimum Data set (MHMDS).

The reporting period for the HES data covered one year from 1st April to 31st March the following year. For example, 2014-15 covered the period 1st April 2014 to 31st March 2015.

Due to the different number of datasets covering different time periods, a number of raw data files were received from NHS Digital (Table 3.3).

Table 3.3: Raw Hospital Episode Statistics (HES) and Mental Health Minimum Data set (MHMDS) file names and descriptions.

Raw HES/MHMDS file name	**Raw HES/MHMDS file description**
LeedsUni_OP_03.txt	Outpatient HES files linked to YSRCCYP cohort for HES years 2003-04 to 2010-11. These separate files had previously been combined into a single STATA file (outpatient_hes_2003_2011_raw.dta)
LeedsUni_OP_04.txt	
LeedsUni_OP_05.txt	
LeedsUni_OP_06.txt	
LeedsUni_OP_07.txt	
LeedsUni_OP_08.txt	
LeedsUni_OP_09.txt	
LeedsUni_OP_10.txt	

extract_Leeds_OP_1112.txt	Outpatient HES files linked to YSRCCYP cohort for HES years 2011-12 to 2014-15. These separate files had previously been combined into a single STATA file (outpatient_hes_2011_2014_raw.dta)
extract_Leeds_OP_1213.txt	
extract_Leeds_OP_1415.txt	
extract_Leeds_AE_0708.txt	A&E HES files linked to YSRCCYP cohort for HES years 2007-08 to 2013-14. These separate files had previously been combined into a single STATA file (A&E_hes_2007_2014_raw.dta)
extract_Leeds_AE_0809.txt	
extract_Leeds_AE_0910.txt	
extract_Leeds_AE_1011.txt	
extract_Leeds_AE_1112.txt	
extract_Leeds_AE_1213.txt	
extract_Leeds_AE_1314.txt	
AE_1415_APPROVED_2319_09052016_8.txt	A&E HES file linked to YSRCCYP cohort for HES year 2014-15.
extract_Leeds_MHLDDS_0607.txt	MHMDS file linked to YSRCCYP cohort for HES year 2006-07.
extract_Leeds_MHLDDS_0708.txt	MHMDS file linked to YSRCCYP cohort for HES year 2007-08.
extract_Leeds_MHLDDS_0809.txt	MHMDS file linked to YSRCCYP cohort for HES year 2008-09.
extract_Leeds_MHLDDS_0910.txt	MHMDS file linked to YSRCCYP cohort for HES year 2009-10.
extract_Leeds_MHLDDS_1011.txt	MHMDS file linked to YSRCCYP cohort for HES year 2010-11.
extract_Leeds_MHLDDS_RECORDS_1112.txt	MHMDS file linked to YSRCCYP cohort for HES year 2011-12.
extract_Leeds_MHLDDS_RECORDS_1213.txt	MHMDS file linked to YSRCCYP cohort for HES year 2012-13.
extract_Leeds_MHLDDS_RECORDS_1314.txt	MHMDS file linked to YSRCCYP cohort for HES year 2013-14.

extract_Leeds_MHLDDS_RECORDS_1415.txt	MHMDS file linked to YSRCCYP cohort for HES year 2014-15.
LeedsUni_APC_97.txt	Inpatient HES files linked to YSRCCYP cohort for HES years 1997-98 to 2016-17 These separate files had previously been combined into a single STATA file (inpatientHES_1997_2017.dta)
LeedsUni_APC_98.txt	
LeedsUni_APC_99.txt	
LeedsUni_APC_00.txt	
LeedsUni_APC_01.txt	
LeedsUni_APC_02.txt	
LeedsUni_APC_03.txt	
LeedsUni_APC_04.txt	
LeedsUni_APC_05.txt	
LeedsUni_APC_06.txt	
LeedsUni_APC_07.txt	
LeedsUni_APC_08.txt	
LeedsUni_APC_09.txt	
LeedsUni_APC_10.txt	
LeedsUni_APC_11.txt	
NIC155843_APC_201199.txt	
NIC155843_APC_201299.txt	
NIC155843_APC_201399.txt	
NIC155843_APC_201499.txt	
NIC155843_APC_201599.txt	
NIC155843_APC_201612.txt	

Some of these separate files for the different HES years had previously been imported into STATA and combined to create single files for the inpatient, outpatient, A&E and MHMDS datasets. However, some additional files required linkage to include all available HES data.

Due to the different timings of the requested HES datasets, different extracts of the YSRCCYP data were sent to NHS Digital for data linkage. Therefore, each HES dataset had to be linked back to the current YSRCCYP data extracted for

this study. This meant that some records could not be linked and were deleted and excluded from analysis. To maximise record linkage between datasets, some identifiers for some HES and MHMDS records were amended. Amending identifiers incorrectly could lead to erroneous results during analysis, so amendments were only performed where duplicate records could be identified before being linked to the current YSRCCYP data.

3.3.5.1 Duplicate records in the Hospital Episode Statistics (HES) datasets.

The HES datasets included identifier variables generated by NHS Digital at record ('attendkey' for the outpatient appointment dataset, 'aekey' for the A&E dataset and 'epikey' for the inpatient admissions dataset) and person ('HESID') level. The datasets also included the YSRCCYP identifiers ('yctr_id' and 'patient_id') provided in the original files sent to NHS Digital for data linkage.

As there were unique characteristics for each HES dataset, cleaning rules were specific to each HES file. However, data cleaning for duplicate records were followed for most HES datasets. Including duplicate records in analysis could lead to overestimations in results. In contrast, incorrectly deleting unique records could mean losing vital information and underestimating results. However, for each HES dataset, there were at most 1% of duplicate records, so any incorrectly deleted or retained records would have minimal impact on the result. Even so, creating an algorithm for dealing with duplicate records was important to minimise any bias.

3.3.5.1.1 Duplicate records assigned to the same Hospital Episode Statistics (HES) record identifier.

For the outpatient and A&E datasets, it was found that some records assigned with different unique HES record identifiers were identified as duplicate records (Table 3.4).

Table 3.4: Record and individual level identifiers for Hospital Episode Statistics (HES) datasets.

	Outpatient	A&E	Inpatient
HES record	attendkey	aekey	epikey
HES person	HESID		

identifier			
YSRCCYP person identifier	yctr_id before 2011 and patient_id after 2011		
Unique record variables	HESID/ YSRCCYP id, date of appointment and treatment speciality	HESID/ YSRCCYP id, date of admission	HESID/ YSRCCYP id, date of admission, diagnosis code

These records were examined individually to ensure only one HESID was linked to one YSRCCYP id.

3.3.5.1.2 One HESID linked to more than one Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) identifier.

Where a HESID was linked to more than one YSRCCYP identifier, records were either deleted or the HESID was amended, depending on the following circumstances:

1. The ‘match rank’ variable in the HES data indicated the quality of matching of individuals between the HES and YSRCCYP datasets. A scoring system between 1 and 8 was used based on a matching algorithm from various identifiable variables (Table 3.5), where a higher score indicated a poorer quality match. Therefore, the record for the YSRCCYP identifier with the highest match rank score for a duplicate HESID would be deleted. For example, record 2 would be deleted in Table 3.6.

Table 3.5: Matching algorithm for individuals in the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) linked to Hospital Episode Statistics (HES).

Match Rank	NHS number	Date of birth	Sex	Postcode	
1	Exact	Exact	Exact	Exact	
2	Exact	Exact	Exact		
3	Exact	Partial	Exact	Exact	
4	Exact	Partial	Exact		
5	Exact			Exact	
6		Exact	Exact	Exact	where NHS number does not contradict the match and date of birth is not 1 January and the POSTCODE is not in the 'ignore' list

7		Exact	Exact	Exact	where NHS number does not contradict the match and date of birth is not 1 January
8	Exact				

Table 3.6: Example of duplicate Hospital Episode Statistics (HES) record deletion using 'match rank'.

	Record id	**HESID**	**patient_id**	**match rank**
Lower match rank score – keep record	1	123456789	abcd	1
Higher match score – delete record	**2**	**123456789**	**efgh**	**8**

2. If the YSRCCYP identifiers were all included in the current extract and the match rank was the same for each YSRCCYP identifier, it could not be determined which person the HES record should be assigned to. Therefore, the HES record remained linked to each person. The HESID was amended so that it remained unique for each person (see example in Table 3.7).

Table 3.7: Example of duplicate Hospital Episode Statistics (HES) record amendment to HESID.

	Record id	**HESID**	**patient_id**	**match rank**
Two records with same HESID and match rank score but different patient_ids	1	123456789	abcd	1
	2	**123456789**	efgh	1
Amended record 2 with a new HESID	1	123456789	abcd	1
	2	**12345678X**	efgh	1

3. Since the YSRCCYP data were sent to NHS Digital for data linkage, some individuals were identified as having more than one YSRCCYP identifier and their duplicate record was removed from the register. In this case, the HES record was linked to the same person with multiple

YSRCCYP identifiers. Therefore, the record with the old YSRCCYP id was deleted (example of original record to amended record in Table 3.8).

Table 3.8: Example of Hospital Episode Statistics (HES) record with YSRCCYP identifier from old extract provided during the linkage process.

	Record id	HESID	patient_id
Original patient_id sent to NHS Digital for data linkage	1	123456789	**aaaa**
Amended patient_id on updated YSRCCYP data	1	123456789	**aaab**

3.3.5.1.3 One Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) identifier linked to more than one HESID.

There was no way to check if these HES records were supposed to match to two different individuals, as the HES identifiable data would match the corresponding YSRCCYP record. However, if there were a method to determine whether these records belonged to separate individuals, there would be no way to be sure which individual the HES record belonged to. Therefore, HESIDs were amended to be the same so only one HESID would match to one YSRCCYP id (example in Table 3.9).

Table 3.9: Example of two HESIDs matched to a single Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) identifier.

	Record id	HESID	patient_id
Two records with same HESID and match rank score but different patient_ids	1	123456789	abcd
	2	**999999999**	abcd
Amended record 2 with a new HESID	1	123456789	abcd
	2	**123456789**	abcd

3.3.5.2 Deleting records before a 5-year follow-up.

Analysis from the YSRCCYP cohort for this study included examining outcomes of LEs for the first diagnosed cancer. Any hospital activity which occurred within the first 5 years of a cancer diagnosis would be regarded as cancer treatment or assessment for relapse. Therefore, only inpatient, outpatient and A&E HES data on or after the 5-year anniversary of the first recorded cancer diagnosis were

included. Consequently, individuals from the YSRCCYP who had a first cancer diagnosis recorded within the last 5 years of the HES dataset time period would not be eligible for analysis due to insufficient follow-up time. The numbers of eligible individuals for analysis by each HES dataset are presented in Table 3.10.

Table 3.10: Total of individuals from the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) eligible for Hospital Episode Statistics (HES) analysis.

	Outpatient and A&E	**MHMDS**	**Inpatient**
Total individuals from YSRCCYP eligible for matching on HES	5,294	7,238	5,833

Analysis using data for mental health admissions included assessment of a mental health episode occurring before the first cancer diagnosis, during the 5-year follow-up period and after the follow-up time. Therefore, all individuals from the YSRCCYP were included in the analysis.

3.3.5.3 Data cleaning for Mental Health Minimum Data set (MHMDS).

The total number of records on the MHMDS raw files are summarised in Table 3.11.

Table 3.11: Total number of records in raw Mental Health Minimum Data set (MHMDS) files.

File year	**Total records**
2006-2007	310
2007-2008	274
2008-2009	222
2009-2010	191
2010-2011	198
2011-2012	208
2012-2013	244
2013-2014	235
2014-2015	256

The raw files were combined and included a total of 2,138 records for 610 individuals. In addition, there were 103 individuals in the HES inpatient data with a mental health admission. There were 62 individuals with records on both the MHMDS and inpatient datasets. Duplicate records were deleted so each individual had only one record. This record included a variable called 'Year of first known psychiatric care', with some records with dates prior to the start of the data collection period (2006-2007). Each individual had a single 'First known contact' date by using the earliest date recorded for the individual from any of their MHMDS episode records. If this field was blank for all records for this individual, the earliest episode start date from any of the recorded episode for these individuals was used instead. For individuals with records on both the MHMDS and inpatient data, the first known contact date would be replaced by a mental health inpatient admission date if this date was prior to the existing first known date recorded on the MHMDS.

In total, 603 individuals with a mental health admission were matched on the YSRCCYP extract. One individual was excluded as their earliest MHMDS date was before their date of birth (Figure 3.8).

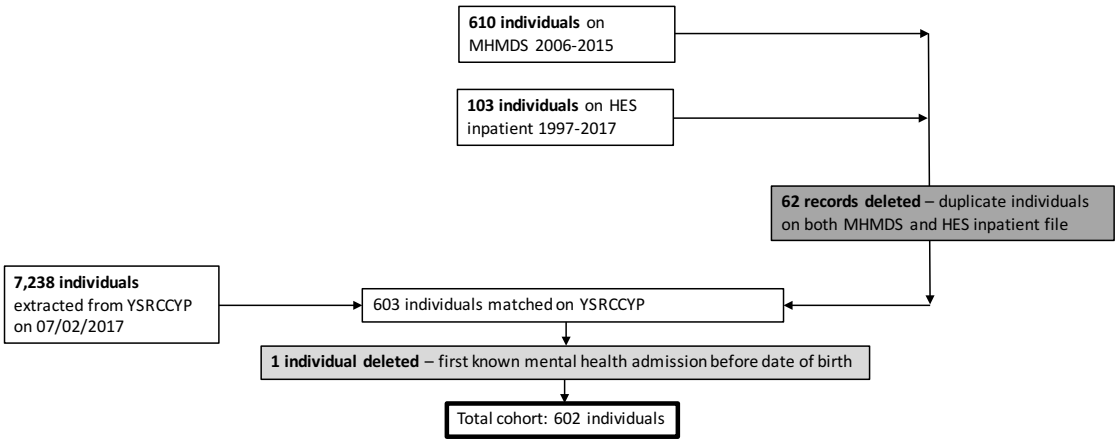


Figure 3.8: Data cleaning for the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) cohort linked to Mental Health Minimum Data set (MHMDS).

3.3.5.4 Data cleaning for outpatient Hospital Episodes Statistics (HES) dataset.

Table 3.12 provides a summary of the total number of outpatient HES records before data cleaning.

Table 3.12: Total of all and unique records in the outpatient Hospital Episode Statistics (HES) data files before data cleaning.

File year	2003-2011	2011-2014	2014-2015
Total records	214,990	104,582	35,858
Total unique ‘attendkey’	214,642	104,315	35,799
Total unique HESIDs	5,773	5,378	4,550
Total unique YSRCCYP id	5,767	5,382	4,556

Figure 3.9 illustrates each data cleaning stage for the outpatient HES data and data linkage to the current YSRCCYP cohort.

There were some individuals who had more than one appointment on the same day. Multiple records on the same day were kept if they were assigned to different treatment specialty groups, as it was possible for individuals to attend two appointments within different departments on the same day.

Some individuals had more than one record of an appointment on the same date and within the same treatment specialty but with different ‘attend’ values, e.g. one record with an ‘attended’ value and the other record with a ‘did not attend’ flag. In this case, the record with the ‘attended’ value would be kept and the ‘did not attend’ record would be deleted. This was because there would be no possible way of checking which record was correct and as most people were likely to have attended the appointment, ‘attended’ was chosen as the default option.

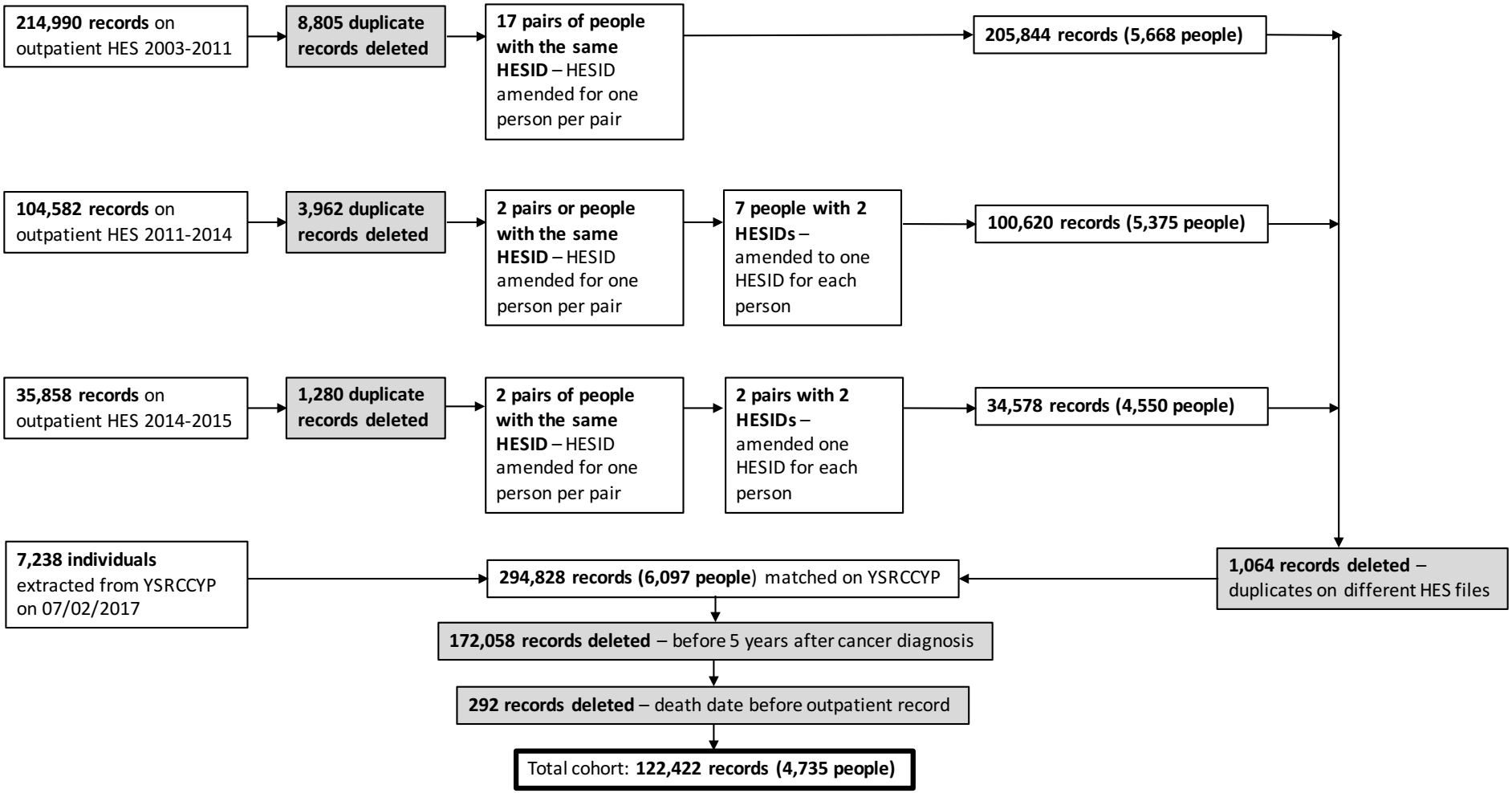


Figure 3.9: Data cleaning for the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) cohort linked to Hospital Episode Statistics (HES) outpatient data.

3.3.5.5 Data cleaning for inpatient Hospital Episode Statistics (HES) dataset.

Each record on the inpatient HES dataset represented an episode of hospitalisation under one consultant. A continuous inpatient spell (CIPS) consisted of multiple episodes for an individual, which may have involved transfers between consultants and/or providers. To be counted as part of the same CIPS, a new episode had to begin within two days of the previous episode ending (258).

For this study, inpatient data were analysed at CIPS level, using the information from the first episode in the CIPS for clinical analysis. CIPS level analysis was preferred over episode analysis to avoid double counting individuals.

The inpatient dataset had previously been cleaned and combined into a single data file, so required minimum data cleaning and processing before data linkage to the YSRCCYP dataset.

There were 104 duplicate 'epikey' records found in the cleaned file. However, it was found that these were not true duplicate records. Unlike the outpatient and A&E datasets, the HES record level identifier was not unique across HES years. Therefore, these records were kept and a new record level identifier was created. Figure 3.10 shows the data cleaning stages and data linkage to the YSRCCYP cohort dataset.

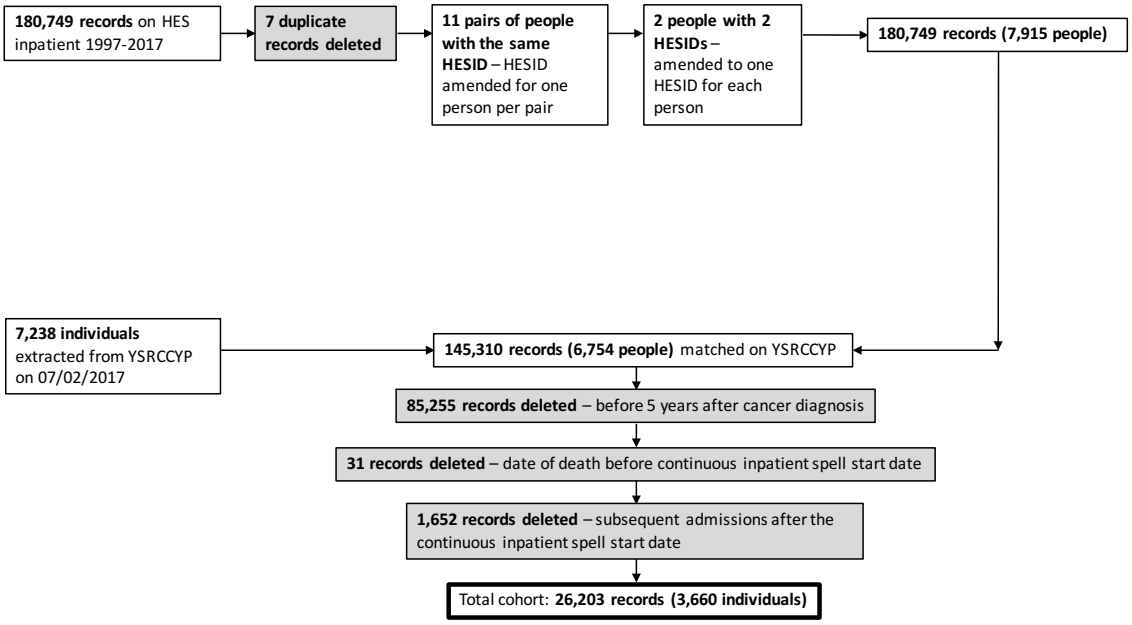


Figure 3.10: Data cleaning for the YSRCCYP cohort linked to inpatient HES data.

3.3.5.6 Data cleaning for accident and emergency (A&E) Hospital Episode Statistics (HES) dataset.

Table 3.13 provides a summary of the total number of A&E HES records before data cleaning.

Table 3.13: Total of all and unique records in the accident and emergency (A&E) Hospital Episode Statistics (HES) data files before data cleaning.

File year	2007-2014	2014-2015
Total records	16,476	2,500
Total unique aekey	16,460	2,496
Total unique HESIDs	4,725	1,585
Total unique YSRCCYP id	4,710	1,588

Figure 3.11 illustrates each data cleaning stage for the A&E HES data and data linkage to the current YSRCCYP cohort.

Some individuals had more than one A&E record on the same day. To ensure that only one A&E attendance was included on a single day, the record with the earliest arrival time was included and any later records were deleted.

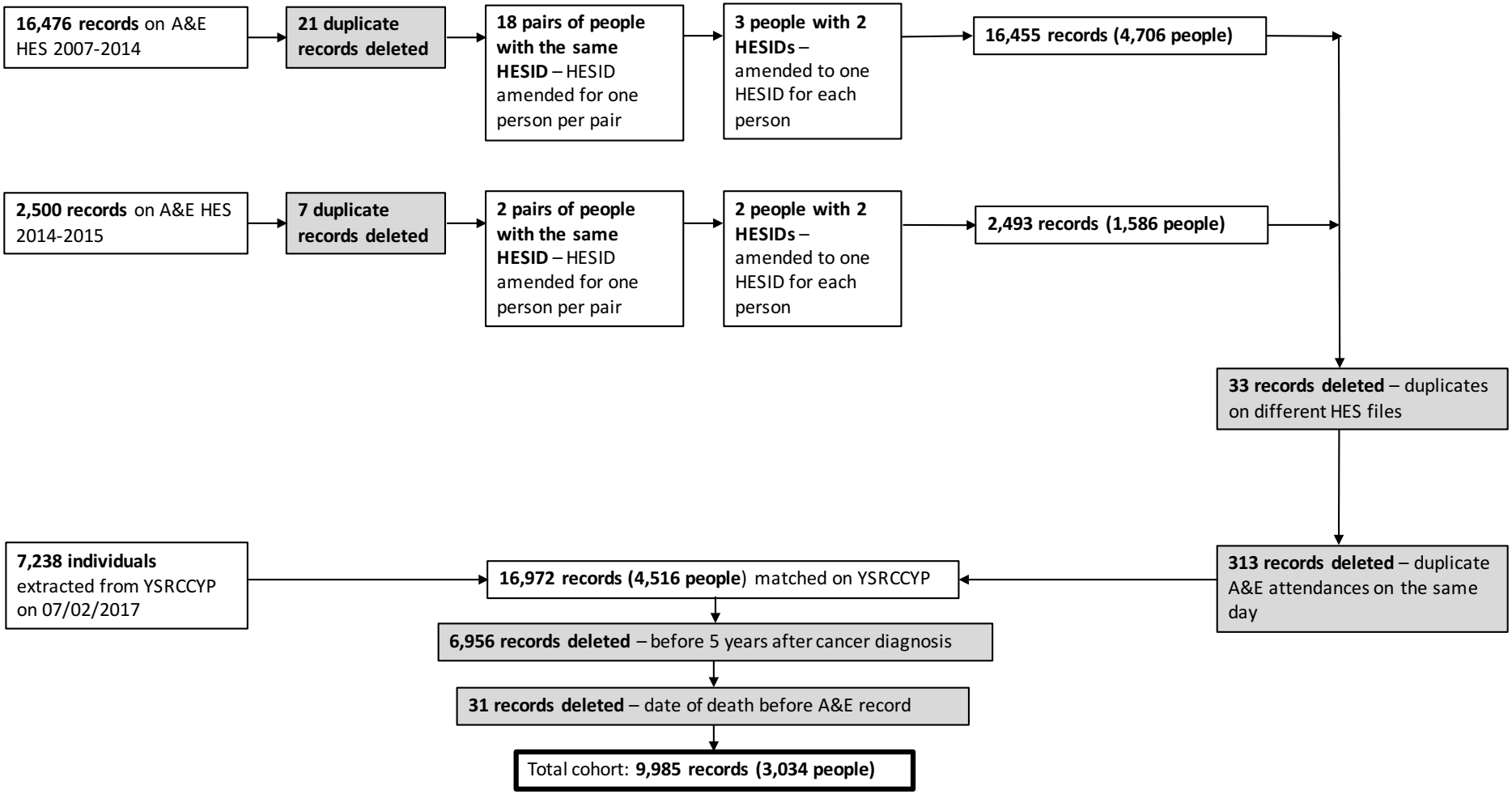


Figure 3.11: Data cleaning for the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) cohort linked to accident and emergency (A&E) data.

3.3.5.7 Combining Hospital Episode Statistics (HES) and Mental Health Minimum Data set (MHMDS).

To determine whether the attendance status of an outpatient appointment was associated with either an A&E attendance or inpatient admission 90 days after the outpatient appointment date, the outpatient HES data were combined with both the A&E and inpatient datasets. The time period coverage of the combined datasets with the total eligible individuals for analysis in the YSRCCYP cohort are presented in Table 3.14.

Table 3.14: Time period coverage of outpatient dataset combined with accident and emergency (A&E) and inpatient datasets.

HES dataset combined with outpatient dataset	Outpatient dataset time period	Linked HES dataset time period	Total eligible individuals
A&E	31/03/2007 to 31/12/2014	01/04/2007 to 31/03/2015	5,221
Inpatient	01/04/2003 to 31/03/2015	02/04/2003 to 29/06/2015	4,735

The MHMDS was combined with the A&E, inpatient and outpatient datasets to determine whether a previous mental health admission was associated with attendance status of an outpatient appointment, attendance to A&E and non-mental health related inpatient admission. All recorded first mental health admission dates before an outpatient, inpatient or A&E attendance were included in the analysis.

3.4 Chapter summary.

This chapter summarises the sources and content of the routine data analysed in this study, alongside the complexities of the dataset-specific cleaning rules before analyses could be carried out. The results of these analyses are described in chapters 4, 5 and 6.

Chapter 4 Mortality in type 1 diabetes.

This chapter outlines the statistical methodology used for analysing data from the YRDCYP linked to ONS death certification data and reports the results from these data analyses. It begins by defining any categorisations of the data and continues with a description of the statistical methods used in the analysis. All analyses were performed using STATA 14 (257).

Mortality was the outcome examined from the YRDCYP cohort. Analysis included the calculation of mortality rates, survival estimates and SMRs by age at death, age at T1D diagnosis, sex, ethnicity and deprivation group. Analysis was performed for all-cause and cause-specific mortality.

4.1 Variable definitions.

4.1.1 Age categories at type 1 diabetes (T1D) diagnosis and at death.

The age variable (attained age and age at death) was grouped into discrete categories to compare health outcomes by age before (under 15 years), during (15 to 29 years) and after (30 and over) the transitional care period. To provide further detailed analysis by age, the YRDCYP was also categorised by 5-year age groups. Individuals from the YRDCYP diagnosed with T1D before the transitional care period are defined as having ‘early T1D onset’. Individuals diagnosed during the transitional care period are defined as having ‘late T1D onset’.

4.1.2 Defining cause-specific mortality categories.

The ICD-10 code for the underlying cause of death variable recorded on the ONS death certification data by a clinical coder was verified by a clinical diabetologist. Table 4.1 tabulates the classification of T1D and non-T1D related underlying causes of deaths and any related subcategories.

T1D-related deaths due to chronic circulatory complications included stroke and ischaemic heart disease (IHD). Any other T1D-related deaths which could not be classified under acute or chronic complications were classed as T1D-related deaths with other/no/unknown complications. This group was not reported on separately in the results section.

Table 4.1: Underlying cause of death classification for cause-specific mortality analysis.

<table>
<tr><th colspan="3">T1D-related deaths</th><th rowspan="2">Non-T1D related deaths</th><th rowspan="7">Other/ unknown causes</th></tr>
<tr><th>Acute complications</th><th>Chronic complications</th><th rowspan="6">Other/no/ unknown complications</th></tr>
<tr><td rowspan="2">Diabetic ketoacidosis (DKA)</td><td rowspan="2">Renal complications</td><td>Respiratory failure</td></tr>
<tr><td>Neoplasms</td></tr>
<tr><td rowspan="3">Severe hypoglycaemia</td><td rowspan="3">Circulatory complications</td><td>Accidents and violence</td></tr>
<tr><td>Mental disorder</td></tr>
<tr><td>Suicide</td></tr>
</table>

4.2 Statistical methodology.

4.2.1 Mortality rates.

Mortality rates were calculated for the whole follow-up period in the YRDCYP. All-cause and cause-specific mortality rates were calculated by dividing the total number of deaths in the YRDCYP by the total person-years of follow-up for the whole cohort. The mortality rate was expressed as the total number of deaths per 10,000 person-years over the cohort time period with 95% confidence intervals calculated using the Poisson distribution. The YRDCYP cohort mortality data met the assumptions of the Poisson distribution where instances of death were independent between individuals and occurred at random. All-cause and cause-specific mortality rates by age, sex, ethnicity and deprivation were calculated for comparison against total cohort rates. This determined whether there were any statistically significant differences for any particular socio-demographic group compared with overall cohort rates.

4.2.2 Survival analysis: Kaplan-Meier estimators.

Although mortality rates were useful to provide a basic descriptive analysis of mortality in the YRDCYP, there was an assumption that these rates were constant over time. Mortality rates could have been calculated by T1D duration periods by different socio-demographic groups. However, grouping T1D duration into discrete categories would limit the accuracy of measuring mortality for specific time points and would also create a large number of mortality rates calculated by subgroups which would be inefficient for analysis.

Survival analysis considered time to event (in this analysis the event was death) and also accounted for censored data. The YRDCYP data included individuals

who were diagnosed with T1D between 1978 and 2013 and were followed-up to death if deaths were recorded before 1st January 2016. For individuals who did not have a death recorded, data were censored on 31st December 2015.

Kaplan-Meier estimates are non-parametric estimators which can be used to produce graphical presentation of the survivor function. The survivor function is the probability of survival past a certain time point. Kaplan-Meier graphs were plotted according to different socio-demographic groups and by different underlying causes of death for the YRDCYP cohort. This allowed for a visual comparison between age at T1D onset, sex, ethnicity, deprivation groups and by underlying causes of death. To test for any overall statistically significant differences between any two Kaplan-Meier curves, univariable log-rank tests were calculated.

Cumulative survival and cumulative mortality over T1D duration can both be plotted using Kaplan-Meier estimates. Both types of graphs represent the same information but are visually different. Cumulative survival graphs show decreasing plots compared with cumulative mortality graphs which show increasing plots. Pocock and colleagues recommended using cumulative mortality plots for data where more than 30% of the cohort have survived. This was so that the y-axis can be truncated after the maximum cumulative mortality estimate rather than truncating the y-axis below the minimum cumulative survival estimate which could lead to misinterpretations when comparing graphs between different groups (259). In this analysis, cumulative mortality graphs were plotted as more than 30% of the YRDCYP survived at the end of the follow-up period.

The cumulative mortality graphs used Kaplan-Meier survival estimates from T1D diagnosis date to either date of death or to 31st December 2015 for individuals with no death certification. T1D duration (time since T1D diagnosis) was used as analysis time as opposed to attained age as attained age would skew plots for the individuals in the late T1D onset group.

4.2.3 Survival analysis: Cox regression models.

Kaplan-Meier estimates with log-rank tests provided useful descriptive analysis for mortality against T1D duration between demographic groups within the YRDCYP. However, Kaplan-Meier estimates could not be adjusted for confounders or other covariates. Therefore, Cox proportional hazards regression modelling was also performed.

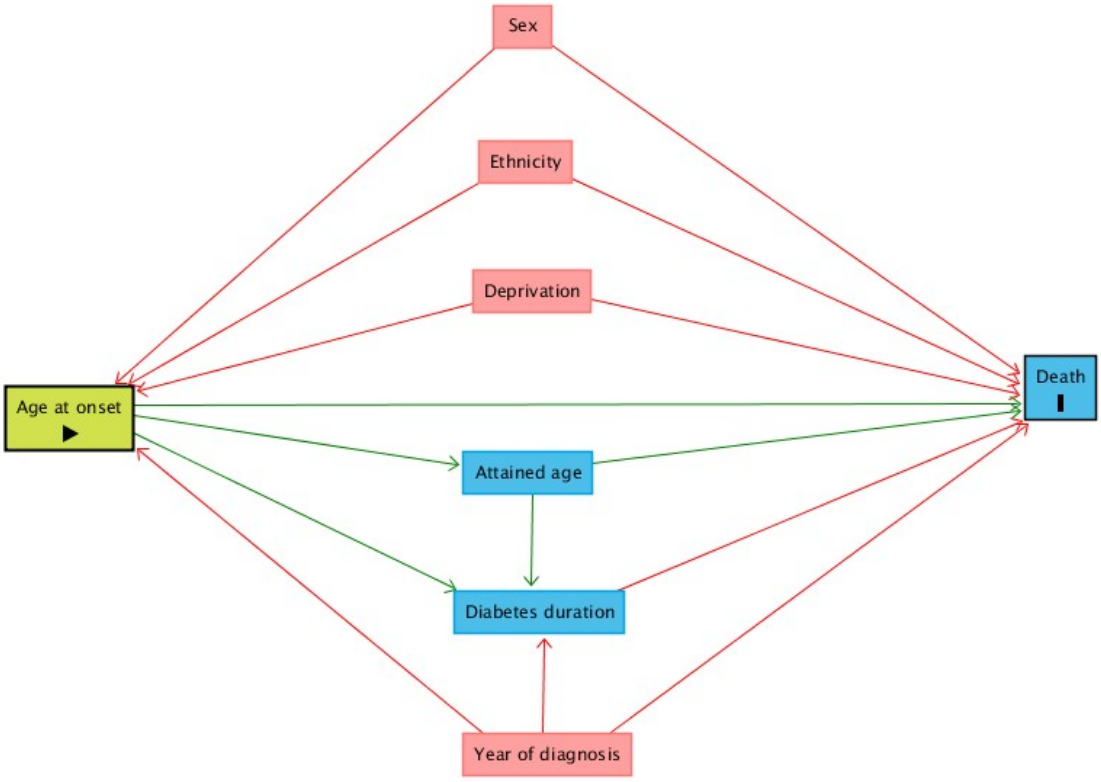
Cox regression is a semiparametric modelling method and can examine the relationship of the hazard function to multiple predictors without the need to determine the underlying hazard function. This has advantages over parametric methods where incorrectly specifying assumptions around the underlying hazard function can lead to inaccurate results. Flexible parametric methods remove some of these constraints around these assumptions and offers direct modelling of the underlying hazard function, which cannot be completed with Cox regression modelling. However, modelling the underlying hazard function was not required for this study, thus Cox regression was the preferred method to assess comparisons of hazards between groups (260).

Cox regression models were run for all-cause mortality. Separate models were also run for T1D-related and non-T1D related deaths. Separate Cox regression models were performed for T1D-related deaths due to acute complications and T1D-related deaths due to chronic complications. No models were run for T1D-related deaths due to DKA, severe hypoglycaemia, renal or circulatory complications. Likewise, there were no separate models run by each non-T1D related underlying cause of death. This was due to the small numbers for these subcategories.

When examining different groups using Cox regression, there is an assumption that the different groups must have proportional hazards over time. This assumption was checked by calculating Schoenfeld residuals to produce an overall global test of the model. If the global test indicated any violation of the proportional hazards assumption, tests by variable were produced to examine any violation at global level (261).

To decide which covariates to include in the Cox regression models, a Directed Acyclic Graph (DAG) was completed (Figure 4.1) based on discussions with and advice from clinical specialists. DAGs capture causal links between exposure and outcome variables to identify the minimal adjustment set of confounder variables for statistical modelling (262). The DAG included age group at T1D onset as the exposure and death as the outcome. Sex, ethnicity and deprivation were found to be confounders and should all have been included in the Cox regression models. However, as more than a fifth of deaths had a missing ethnicity code and there were small numbers of South Asians by underlying cause of death, ethnicity was excluded from the models.

Attained age, diabetes duration and year of diagnosis were found to be mediators. All mediators, except year of diagnosis were excluded from the models. Year of diagnosis was included in the models as a continuous variable as changes in T1D treatment changed during the data collection period, so the year of diagnosis may have influenced the risk of death.



Confounders = sex, ethnicity, deprivation

Mediators = attained age, diabetes duration, year of diagnosis

Figure 4.1: Directed Acyclic Graph (DAG) for Cox regression model for mortality in the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort.

4.2.4 Standardised Mortality Ratios (SMRs).

To compare mortality in the YRDCYP against the general population, SMRs were calculated. SMRs are a ratio between the observed and the expected number of deaths in the YRDCYP. The expected numbers of deaths were calculated by applying England and Wales all-cause and cause-specific mortality rates to the YRDCYP cohort using population and mortality data between 1978 and 2014. These data were available by 5-year age group and sex (263). The Poisson distribution was used to calculate the SMR 95% confidence intervals.

It would have been preferable to use the geographical region of the former YRHA as the general population for the early T1D onset group and the West Yorkshire region as the general population for the late T1D onset group (191). However, population and mortality data for the general population at this level for the required years and demographic breakdowns were unavailable.

The England and Wales population and mortality rates included individuals with T1D, which may have caused bias in the SMRs. However, as the prevalence of T1D was less than 0.5% (264) this bias in SMRs was low according to Jones and Swerdlow's (1998) recalculated unbiased SMRs (265).

As the general population does not die from T1D-related underlying causes, SMRs by T1D-related deaths were not calculated. Calculating SMRs using the same standardisation for T1D-related deaths would lead to inflated SMRs for the YRDCYP cohort. However, individuals who died from a T1D-related underlying cause were included in all-cause mortality SMR calculations. Any analysis for T1D-related deaths was limited to mortality rates and survival analysis.

4.3 Results of analysis from the Yorkshire Register of Diabetes in Children and Young People (YRDCYP).

4.3.1 Demographics.

The YRDCYP cohort included a total of 5,498 individuals (100,959 person-years of follow-up) (Table 4.2). More individuals with early T1D onset were diagnosed in later years, with a third diagnosed from 1999 with 16 years or less follow-up time. This contributed to similar median follow-up times per person between the early (17.7 years (range 1.5 to 38 years)) and the late T1D onset group (16.3 years (range 0.3 to 25 years)), despite data collection beginning 13 years earlier in the early T1D onset group.

The majority of the YRDCYP (n=3,712; 67.5% of the total cohort) were classified as being of white or South Asian ethnic origin. There were 14 individuals who were classified with either black or East Asian ethnicity. These individuals have been included under the 'Other' ethnicity category. In the South Asian/Other group, 75.3% were classified in the most deprived fifth. This is compared with 24.9% of individuals with white ethnic origin who were classified in the most deprived fifth (Table 4.3).

Table 4.2: Number (and percentage) of individuals and person-years by age at type 1 diabetes (T1D) diagnosis and sex.

		Age at T1D diagnosis		Sex			Total
		0 to 14 years	**15 to 29 years**	**Males**	**Females**	**Unknown**	
Total individuals		4,382 (79.7%)	1,116 (20.3%)	2,970 (54.0%)	2,527 (46.0%)	1 (0.0%)	5,498
Total person-years		83,097.2 (82.3%)	17,861.9 (17.7%)	53,854.7 (53.3%)	47,097.5 (46.7%)	6.8 (0.0%)	100,959.0
Mean person-years per individual		19.0	16.0	18.1	18.6	-	18.4
Median person-years per individual		17.7	16.3	17.1	17.5	-	17.3
Age at T1D diagnosis	0 to 14 years (early onset)	-	-	2,276 (51.9%)	2,105 (48%)	1 (0.0%)	4,382
	15 to 29 years (late onset)	-	-	694 (62.2%)	422 (37.8%)	-	1,116
Sex	Males	2,276 (76.6%)	694 (23.4%)	-	-	-	2,970
	Females	2,105 (83.3%)	422 (16.7%)	-	-	-	2,527
	Unknown	1 (100.0%)	-	-	-	-	1
Ethnicity	White	2,707 (81.0%)	636 (19%)	1,762 (52.7%)	1,581 (47.3%)	-	3,343
	South Asian/Other	272 (72.9%)	101 (27.1%)	192 (51.5%)	181 (48.5%)	-	373
	Unknown	1,403 (78.7%)	379 (21.3%)	1,016 (57.0%)	765 (42.9%)	1 (0.0%)	1,782
Deprivation	Most deprived fifth	1,248 (81.5%)	284 (18.5%)	822 (53.7%)	710 (46.3%)	-	1,532
	2nd most deprived fifth	1,048 (82.5%)	222 (17.5%)	677 (53.3%)	593 (46.7%)	-	1,270
	3rd most deprived fifth	902 (81.2%)	209 (18.8%)	592 (53.3%)	518 (46.6%)	1 (0.0%)	1,111
	2nd least deprived fifth	675 (77.1%)	200 (22.9%)	473 (54.1%)	402 (45.9%)	-	875

	Least deprived fifth	509 (71.7%)	201 (28.3%)	406 (57.2%)	304 (42.8%)	-	710

Table 4.3: Number (and percentage) of individuals and person-years by deprivation.

		Deprivation					Total
		Most deprived fifth	**2nd most deprived fifth**	**3rd most deprived fifth**	**2nd least deprived fifth**	**Least deprived fifth**	
Total individuals		1,532 (27.9%)	1,270 (23.1%)	1,111 (20.2%)	875 (15.9%)	710 (12.9%)	5,498
Total person-years		27,877.5 (27.6%)	22,917 (22.7%)	20,616.6 (20.4%)	16,428.6 (16.3%)	13,119.4 (13.0%)	100,959.0
Mean person-years per individual		18.2	18	18.6	18.8	18.5	18.4
Median person-years per individual		17.4	16.5	17.5	17.9	17.4	17.3
Age at T1D diagnosis	0 to 14 years (early onset)	1,248 (28.5%)	1,048 (23.9%)	902 (20.6%)	675 (15.4%)	509 (11.6%)	4,382
	15 to 29 years (late onset)	284 (25.4%)	222 (19.9%)	209 (18.7%)	200 (17.9%)	201 (18.0%)	1,116
Sex	Males	822 (27.7%)	677 (22.8%)	592 (19.9%)	473 (15.9%)	406 (13.7%)	2,970
	Females	710 (28.1%)	593 (23.5%)	518 (20.5%)	402 (15.9%)	304 (12.0%)	2,527
	Unknown	-	-	1 (0%)	-	-	1
Ethnicity	White	831 (24.9%)	825 (24.7%)	709 (21.2%)	563 (16.8%)	415 (12.4%)	3,343
	South Asian/Other	281 (75.3%)	53 (14.2%)	22 (5.9%)	13 (3.5%)	4 (1.1%)	373
	Unknown	420 (23.6%)	392 (22.0%)	380 (21.3%)	299 (16.8%)	291 (16.3%)	1,782

4.3.2 Deaths by cause-specific mortality before and after clinical validation.

There were 229 (4.2% of the cohort) death certificates, of which 123 mentioned diabetes of any type; forty-eight specifically mentioned T1D. After clinical validation of underlying cause of death, 53 (23.1%) deaths were reclassified. The majority were reclassified with T1D (n=119; 52%), including 10 deaths originally classified as being due to IHD and 5 deaths originally classified under renal disease. These deaths were reclassified as T1D-related deaths due to chronic complications. Twenty-three deaths which were originally coded as 'Other/Unknown', were re-classified as deaths due to 'Accidents and violence' after clinical validation (Table 4.4).

Table 4.4: Classification of underlying cause of death between the original clinical coder at the Office for National Statistics (ONS) and specialist diabetologist.

Underlying cause of death	Clinical coder (% of total deaths)	Specialist clinician (% of total deaths)
Diabetes*	85 (37.1%)	119 (52.0%)
Ischemic heart disease (IHD)	10 (4.4%)	0
Stroke	1 (0.4%)	1 (0.4%)
Renal disease	5 (2.2%)	0
Respiratory failure	12 (5.2%)	7 (3.1%)
Neoplasms	13 (5.7%)	13 (5.7%)
Mental disorder	10 (4.4%)	10 (4.4%)
Accidents and violence	18 (7.9%)	27 (11.8%)
Suicide	14 (6.1%)	14 (6.1%)
Other/Unknown	61 (26.6%)	38 (16.6%)
Total	229	229

*Specified, non-specified or unknown diabetes type for clinical coder. T1D for specialist clinician.

Of the 119 deaths with an underlying cause of T1D, fifty-six deaths (around a quarter of all deaths) were due to T1D-related acute complications (DKA and severe hypoglycaemia). There were twice as many deaths due to DKA compared with severe hypoglycaemia. For T1D-related deaths due to chronic complications, there were 16 deaths due to renal complications and 17 deaths due to circulatory complications (16 deaths due to IHD and 1 death due to stroke) (Table 4.5).

The accidents and violence category included the highest percentage of deaths for non-T1D related mortality (Table 4.6).

Table 4.5: Number of type 1 diabetes (T1D) related deaths (and percentage of total deaths) by socio-demographic groups.

		All T1D-related deaths	Acute complications		Chronic complications		Total deaths
			DKA	Hypoglycaemia	Renal	Circulatory	
Total individuals		119 (52%)	38 (16.6%)	18 (7.9%)	16 (7%)	17 (7%)	229
Age at T1D diagnosis	0 to 14 years (early onset)	88 (56.4%)	28 (17.9%)	15 (9.6%)	11 (7.1%)	15 (9.6%)	156
	15 to 29 years (late onset)	31 (42.5%)	10 (13.7%)	3 (4.1%)	5 (6.8%)	2 (2.7%)	73
Sex	Males	83 (50.3%)	26 (15.8%)	12 (7.3%)	8 (4.8%)	13 (7.9%)	165
	Females	36 (56.3%)	12 (18.8%)	6 (9.4%)	8 (12.5%)	4 (6.3%)	64
Ethnicity	White	85 (50.3%)	30 (17.8%)	13 (7.7%)	10 (5.9%)	11 (6.5%)	169
	South Asian/Other	2 (22.2%)	0	0	1 (11.1%)	0	9
	Unknown	32 (62.7%)	8 (15.7%)	5 (9.8%)	5 (9.8%)	6 (11.8%)	51
Deprivation	Most deprived fifth	30 (44.1%)	11 (16.2%)	2 (2.9%)	3 (4.4%)	4 (5.9%)	68
	2nd most deprived fifth	33 (58.9%)	2 (33.3%)	5 (8.9%)	7 (12.5%)	5 (8.9%)	56
	3rd most deprived fifth	27 (57.4%)	13 (50%)	6 (12.8%)	4 (8.5%)	2 (4.3%)	47
	2nd least deprived fifth	16 (34%)	1 (2.9%)	2 (6.1%)	1 (3%)	4 (12.1%)	33
	Least deprived fifth	13 (39.4%)	5 (10.4%)	3 (12%)	1 (4%)	2 (8%)	25
Age at death	5 to 9	1 (33.3%)	1 (33.3%)	0	0	0	3
	10 to 14	2 (33.3%)	2 (33.3%)	0	0	0	6
	15 to 19	17 (65.4%)	13 (50%)	2 (7.7%)	0	0	26
	20 to 24	13 (38.2%)	1 (2.9%)	4 (11.8%)	1 (2.9%)	2 (5.9%)	34
	25 to 29	21 (43.8%)	5 (10.4%)	5 (10.4%)	3 (6.3%)	2 (4.2%)	48
	30 to 34	22 (52.4%)	8 (19%)	7 (16.7%)	2 (4.8%)	3 (7.1%)	42
	35 to 39	24 (64.9%)	6 (16.2%)	14 (37.8%)	8 (21.6%)	4 (10.8%)	37
	40 to 44	11 (52.4%)	1 (4.8%)	5 (23.8%)	1 (4.8%)	3 (14.3%)	21
	45 to 49	6 (66.7%)	0	5 (55.6%)	1 (11.1%)	2 (22.2%)	9
	50 and over	2 (66.7%)	1 (33.3%)	1 (33.3%)	0	1 (33.3%)	3

Table 4.6: Number of non-type 1 diabetes (T1D) related deaths (and percentage of total deaths) by socio-demographic groups.

		All non-T1D related deaths	Respiratory failure	Neoplasms	Accidents and violence	Mental disorder	Suicide	Other/ Unknown	Total deaths
Total individuals		71 (31%)	7 (3.1%)	13 (5.7%)	27 (11.8%)	10 (4.4%)	14 (6.1%)	39 (17%)	229
Age at T1D diagnosis	0 to 14 years (early onset)	41 (26.3%)	5 (3.2%)	7 (4.5%)	18 (11.5%)	3 (1.9%)	8 (5.1%)	27 (17.3%)	156
	15 to 29 years (late onset)	30 (41.1%)	2 (2.7%)	6 (8.2%)	9 (12.3%)	7 (9.6%)	6 (8.2%)	12 (16.4%)	73
Sex	Males	53 (32.1%)	5 (3%)	9 (5.5%)	19 (11.5%)	7 (4.2%)	13 (7.9%)	29 (17.6%)	165
	Females	18 (28.1%)	2 (3.1%)	4 (6.3%)	8 (12.5%)	3 (4.7%)	1 (1.6%)	10 (15.6%)	64
Ethnicity	White	52 (30.8%)	5 (3%)	7 (4.1%)	24 (14.2%)	9 (5.3%)	7 (4.1%)	32 (18.9%)	169
	South Asian/Other	7 (77.8%)	2 (22.2%)	3 (33.3%)	1 (11.1%)	1 (11.1%)	0	0	9
	Unknown	12 (23.5%)	0	3 (5.9%)	2 (3.9%)	0	7 (13.7%)	7 (13.7%)	51
Deprivation	Most deprived fifth	24 (35.3%)	3 (4.4%)	5 (7.4%)	10 (14.7%)	4 (5.9%)	2 (2.9%)	14 (20.6%)	68
	2nd most deprived fifth	14 (25%)	3 (5.4%)	2 (3.6%)	4 (7.1%)	1 (1.8%)	4 (7.1%)	9 (16.1%)	56
	3rd most deprived fifth	12 (25.5%)	1 (2.1%)	2 (0%)	4 (8.5%)	3 (6.4%)	2 (4.3%)	8 (17%)	47
	2nd least deprived fifth	12 (36.4%)	0 (0%)	2 (6.1%)	6 (18.2%)	1 (3%)	3 (9.1%)	5 (15.2%)	33
	Least deprived fifth	9 (36%)	0 (0%)	2 (8%)	3 (12%)	1 (4%)	3 (12%)	3 (12%)	25
Age at death	5 to 9	1 (33.3%)	0	1 (33.3%)	0	0	0	1 (33.3%)	3
	10 to 14	3 (50%)	0	1 (16.7%)	2 (33.3%)	0	0	1 (16.7%)	6
	15 to 19	7 (26.9%)	1 (3.8%)	0	5 (19.2%)	0	1 (3.8%)	2 (7.7%)	26
	20 to 24	15 (44.1%)	4 (11.8%)	0	6 (17.6%)	2 (5.9%)	3 (8.8%)	6 (17.6%)	34
	25 to 29	19 (39.6%)	0	3 (6.3%)	8 (16.7%)	6 (12.5%)	2 (4.2%)	8 (16.7%)	48
	30 to 34	12 (28.6%)	2 (4.8%)	2 (4.8%)	4 (9.5%)	2 (4.8%)	2 (4.8%)	8 (19%)	42
	35 to 39	6 (16.2%)	0	1 (2.7%)	1 (2.7%)	0	4 (10.8%)	7 (18.9%)	37
	40 to 44	7 (33.3%)	0	4 (19%)	1 (4.8%)	0	2 (9.5%)	3 (14.3%)	21
	45 to 49	1 (11.1%)	0	1 (11.1%)	0	0	0	2 (22.2%)	9
	50 and over	0 (0%)	0	0	0	0	0	1 (33.3%)	3

4.3.3 Mortality analysis for the overall Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort.

4.3.3.1 Mortality rates.

The overall mortality rate for all-cause mortality was 2.27 per 1,000 person-years (95% CI 1.99 to 2.58) (Table 4.7).

For T1D-related deaths due to acute complications, DKA had the highest mortality rate and was significantly higher compared with severe hypoglycaemia, which had the lowest mortality rate of all T1D-related causes. The DKA mortality rate was also significantly higher than the mortality rate for T1D-related deaths due to renal and circulatory chronic complications. No statistically significant difference in mortality rates was found between T1D-related deaths due to renal and circulatory chronic complications (Table 4.7).

There were no statistically significant differences in mortality rates between T1D-related and non-T1D related deaths. Accidents and violence had the highest mortality rate for non-T1D related deaths and was significantly higher than the mortality rate for deaths due to respiratory failure, which had the lowest mortality rate for non-T1D related causes (Table 4.8).

Table 4.7: Mortality rates (and 95% CI) per 10,000 person-years for type 1 diabetes (T1D) related deaths by socio-demographic groups.

		All deaths	T1D –related deaths				
			All deaths	DKA	Severe hypoglycaemia	Renal	Circulatory
Total cohort		2.27 (1.99 to 2.58)	1.18 (0.98 to 1.41)	0.42 (0.31 to 0.56)	0.14 (0.08 to 0.23)	0.16 (0.10 to 0.26)	0.17 (0.10 to 0.27)
Age at T1D diagnosis	0 to 14 years (early onset)	**1.88 (1.60 to 2.20)⁺**	1.06 (0.86 to 1.31)	0.37 (0.26 to 0.53)	0.14 (0.08 to 0.25)	0.13 (0.07 to 0.24)	0.18 (0.11 to 0.30)
	15 to 29 years (late onset)	**4.09 (3.25 to 5.14)**⁺**	1.74 (1.22 to 2.47)	0.62 (0.34 to 1.11)	0.11 (0.03 to 0.45)	0.28 (0.12 to 0.67)	0.11 (0.03 to 0.45)
Sex	Males	**3.06 (2.63 to 3.57)**⁺**	1.54 (1.24 to 1.91)	0.54 (0.37 to 0.77)	0.17 (0.09 to 0.32)	0.15 (0.07 to 0.30)	0.24 (0.14 to 0.42)
	Females	**1.36 (1.06 to 1.74)*⁺**	0.76 (0.55 to 1.06)	0.28 (0.16 to 0.48)	0.11 (0.04 to 0.26)	0.17 (0.08 to 0.34)	0.08 (0.03 to 0.23)
Ethnicity	White	**3.39 (2.92 to 3.94)****	1.71 (1.38 to 2.11)	0.66 (0.47 to 0.93)	0.20 (0.11 to 0.37)	0.20 (0.11 to 0.37)	0.22 (0.12 to 0.40)
	South Asian/Other	1.60 (0.83 to 3.08)	0.36 (0.09 to 1.42)	-	-	0.18 (0.03 to 1.26)	-
	Unknown	-	-	-	-	-	-
Deprivation	Most deprived fifth	2.44 (1.92 to 3.09)	1.08 (0.75 to 1.54)	0.39 (0.22 to 0.71)	0.07 (0.02 to 0.29)	0.11 (0.03 to 0.33)	0.14 (0.05 to 0.38)
	2nd most deprived fifth	2.44 (1.88 to 3.18)	1.44 (1.02 to 2.03)	0.44 (0.23 to 0.81)	0.22 (0.09 to 0.52)	0.31 (0.15 to 0.64)	0.22 (0.09 to 0.52)
	3rd most deprived fifth	2.28 (1.71 to 3.03)	1.31 (0.90 to 1.91)	0.49 (0.26 to 0.90)	0.15 (0.05 to 0.45)	0.19 (0.07 to 0.52)	0.10 (0.02 to 0.39)
	2nd least deprived fifth	2.01 (1.43 to 2.83)	0.97 (0.60 to 1.59)	0.43 (0.20 to 0.89)	0.06 (0.01 to 0.43)	0.06 (0.01 to 0.43)	0.24 (0.09 to 0.65)
	Least deprived fifth	1.91 (1.29 to 2.82)	0.99 (0.58 to 1.71)	0.30 (0.11 to 0.81)	0.23 (0.07 to 0.71)	0.08 (0.01 to 0.54)	0.15 (0.04 to 0.61)

*Statistically significantly lower than the mortality rate for the total cohort.
**Statistically significantly higher than the mortality rate for the total cohort.
⁺Statistically significantly different from other another group within the same socio-demographic variable.

Table 4.8: Mortality rates (and 95% CI) per 10,000 person-years for non-type 1 diabetes (T1D) related deaths by socio-demographic groups.

		Non-T1D related deaths					
		All deaths	**Respiratory failure**	**Neoplasms**	**Accidents and violence**	**Mental disorder**	**Suicide**
Total cohort		1.09 (0.9 to 1.31)	0.07 (0.03 to 0.15)	0.13 (0.07 to 0.22)	0.27 (0.18 to 0.39)	0.10 (0.05 to 0.18)	0.14 (0.08 to 0.23)
Age at T1D diagnosis	0 to 14 years (early onset)	**0.82 (0.65 to 1.04)+**	0.06 (0.03 to 0.14)	0.08 (0.04 to 0.18)	0.22 (0.14 to 0.34)	**0.04 (0.01 to 0.11)+**	0.10 (0.05 to 0.19)
	15 to 29 years (late onset)	**2.35 (1.74 to 3.18)**+**	0.11 (0.03 to 0.45)	0.34 (0.15 to 0.75)	0.5 (0.26 to 0.97)	**0.39 (0.19 to 0.82)+**	0.34 (0.15 to 0.75)
Sex	Males	**1.52 (1.23 to 1.89)+**	0.09 (0.04 to 0.22)	0.17 (0.09 to 0.32)	0.35 (0.23 to 0.55)	0.13 (0.06 to 0.27)	0.24 (0.14 to 0.42)
	Females	**0.59 (0.41 to 0.86)*+**	0.04 (0.01 to 0.17)	0.08 (0.03 to 0.23)	0.17 (0.08 to 0.34)	0.06 (0.02 to 0.2)	0.02 (0 to 0.15)
Ethnicity	White	**1.69 (1.36 to 2.09)****	0.1 (0.04 to 0.24)	0.14 (0.07 to 0.29)	**0.48 (0.32 to 0.72)+**	0.18 (0.09 to 0.35)	0.14 (0.07 to 0.29)
	South Asian/Other	1.24 (0.59 to 2.61)	0.36 (0.09 to 1.42)	0.53 (0.17 to 1.65)	0.18 (0.03 to 1.26)	0.18 (0.03 to 1.26)	-
	Unknown	-	-	0.07 (0.02 to 0.2)	**0.04 (0.01 to 0.18)*+**	-	0.15 (0.07 to 0.32)
Deprivation	Most deprived fifth	1.36 (0.99 to 1.87)	0.11 (0.03 to 0.33)	0.18 (0.07 to 0.43)	0.36 (0.19 to 0.67)	0.14 (0.05 to 0.38)	0.07 (0.02 to 0.29)
	2nd most deprived fifth	1 (0.67 to 1.51)	0.13 (0.04 to 0.41)	0.09 (0.02 to 0.35)	0.17 (0.07 to 0.47)	0.04 (0.01 to 0.31)	0.17 (0.07 to 0.47)
	3rd most deprived fifth	0.97 (0.63 to 1.5)	0.05 (0.01 to 0.34)	0.1 (0.02 to 0.39)	0.19 (0.07 to 0.52)	0.15 (0.05 to 0.45)	0.10 (0.02 to 0.39)
	2nd least deprived fifth	1.03 (0.64 to 1.66)	-	0.12 (0.03 to 0.49)	0.37 (0.16 to 0.81)	0.06 (0.01 to 0.43)	0.18 (0.06 to 0.57)
	Least deprived fifth	0.91 (0.52 to 1.61)	-	0.15 (0.04 to 0.61)	0.23 (0.07 to 0.71)	0.08 (0.01 to 0.54)	0.23 (0.07 to 0.71)

*Statistically significantly lower than the mortality rate for the total cohort.
**Statistically significantly higher than the mortality rate for the total cohort.
+Statistically significantly different from other another group within the same socio-demographic variable.

4.3.3.2 Survival analysis.

Although there was no statistically significant difference in mortality rates between T1D-related and non-T1D related deaths, Kaplan-Meier curves indicated that there was significantly higher cumulative mortality for non-T1D related compared with T1D-related mortality over T1D duration (Figure 4.2).

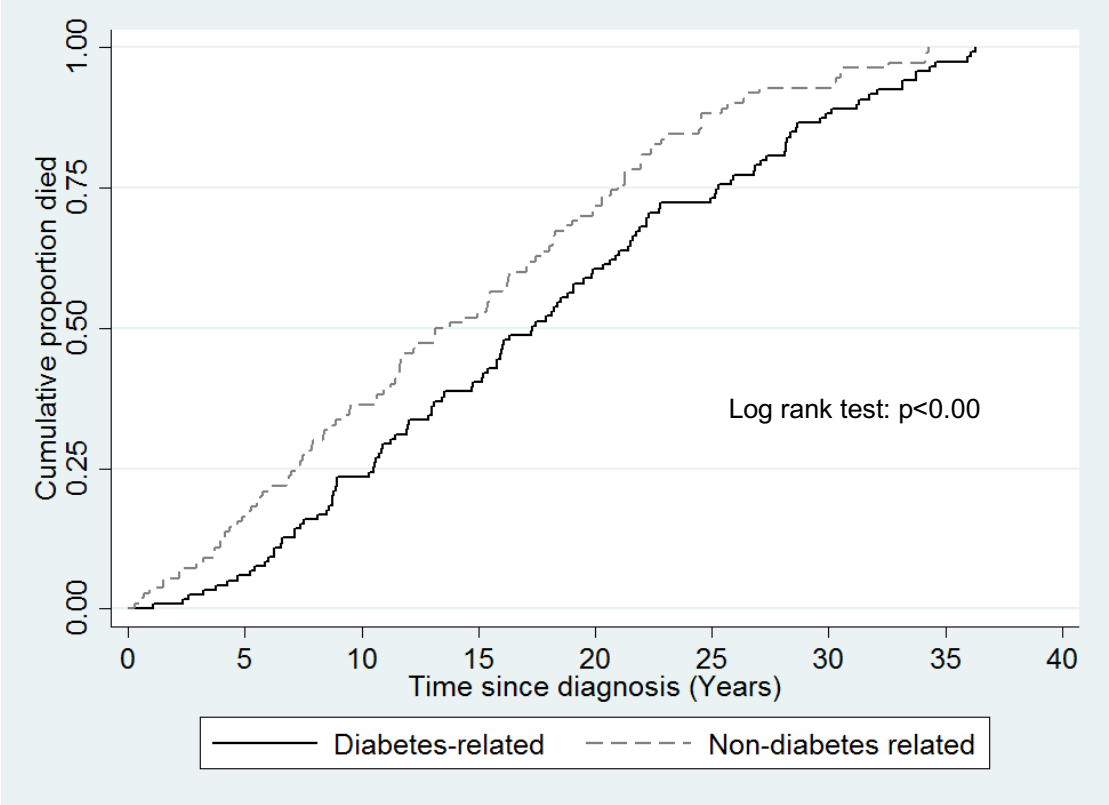


Figure 4.2: Cumulative mortality curves by type 1 diabetes (T1D) and non-T1D related deaths.

Figure 4.3 showed a significantly higher cumulative mortality over T1D duration for deaths due to T1D-related acute complications compared with chronic complications.

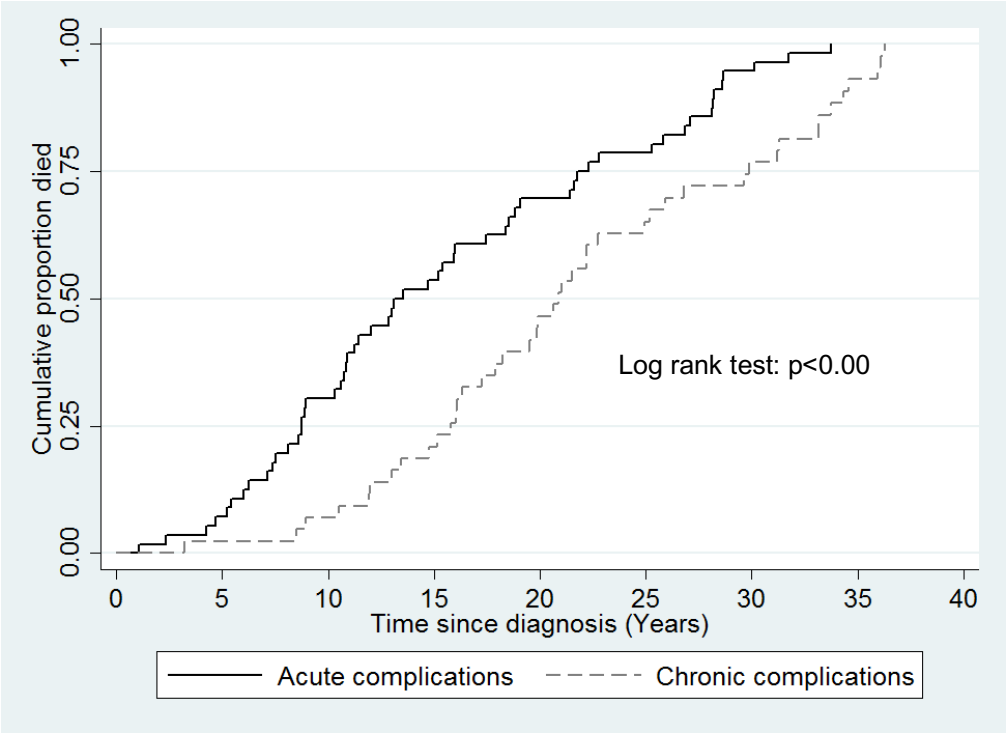


Figure 4.3: Cumulative mortality curves for type 1 diabetes (T1D) related deaths due to acute and chronic complications.

Figure 4.4 showed the cumulative mortality curves for T1D-related deaths due to DKA and severe hypoglycaemia. This showed a higher cumulative mortality for T1D-related deaths due to DKA from around 6 years T1D duration.

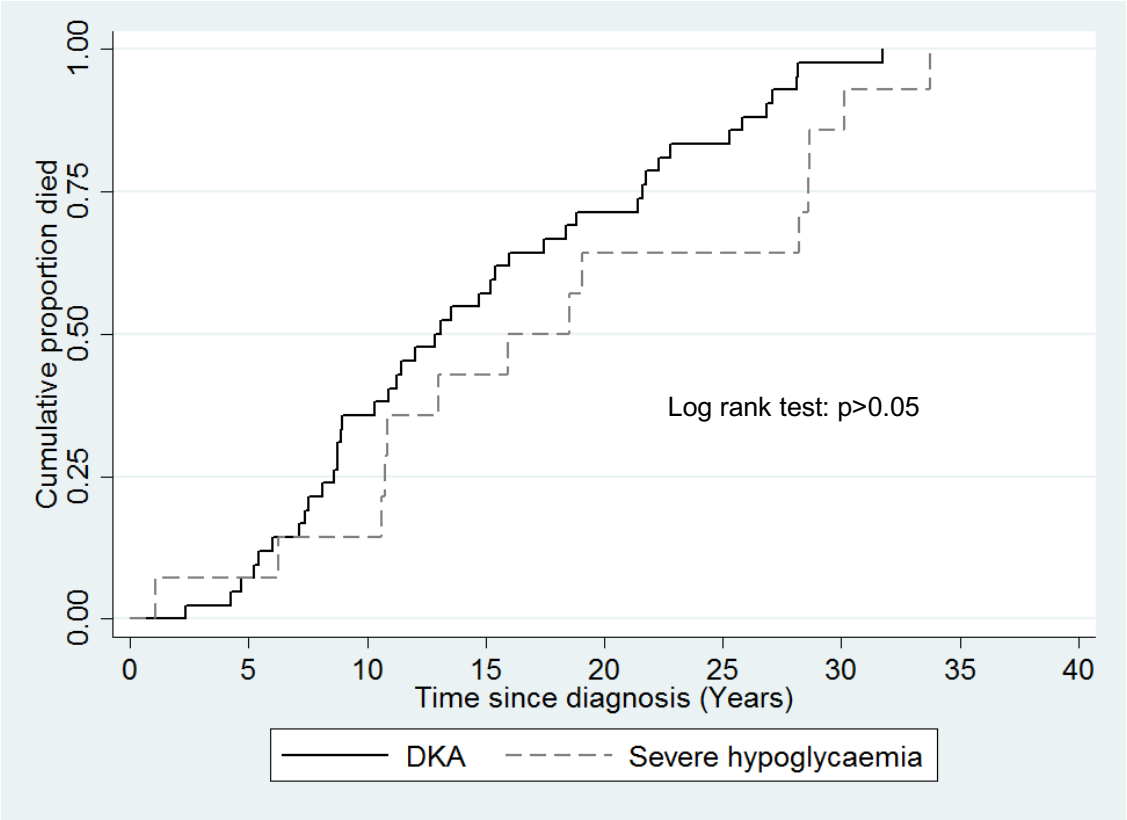


Figure 4.4: Cumulative mortality curves by diabetic ketoacidosis (DKA) and severe hypoglycaemia.

Figure 4.5 showed the cumulative mortality curves for T1D-related deaths due to renal, circulatory and other complications. T1D-related deaths due to renal complications shows higher mortality compared with T1D-related deaths due to circulatory complications from around 13 years of T1D duration.

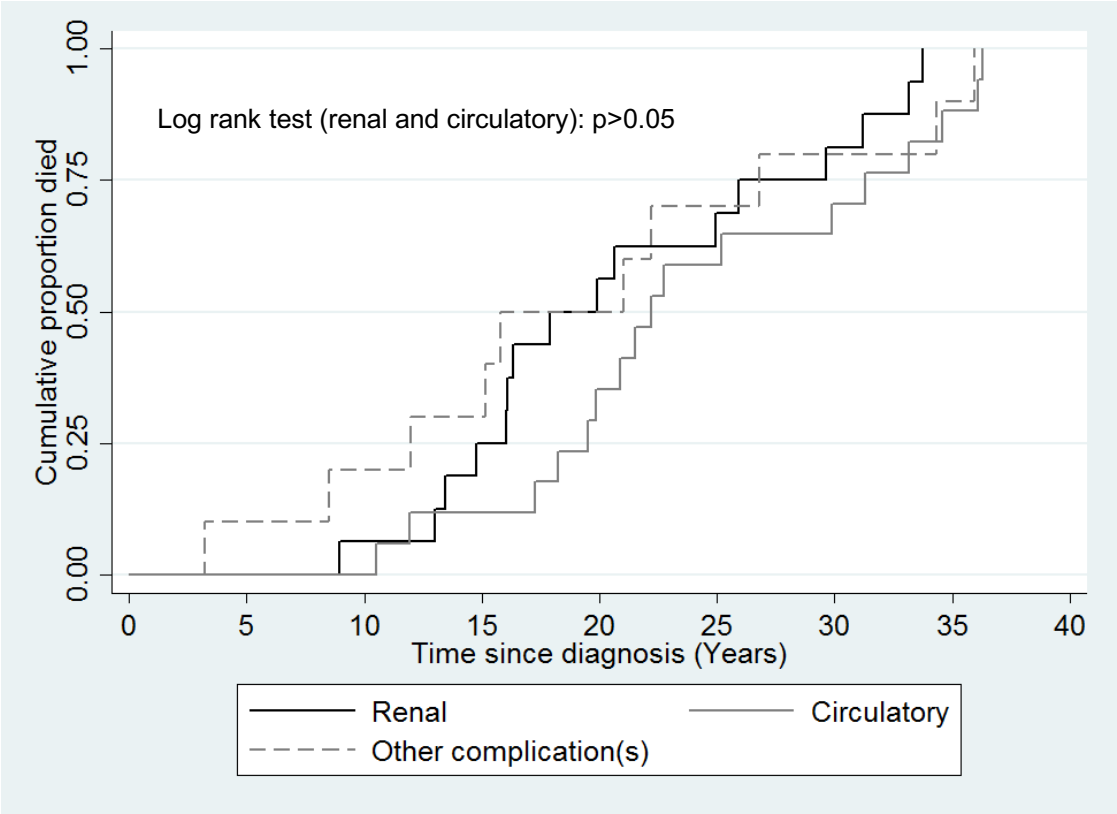


Figure 4.5: Cumulative mortality curves by renal, circulatory and other deaths due to type 1 diabetes (T1D) related complications.

When examining Kaplan-Meier cumulative mortality curves by non-T1D related underlying causes of death, mental disorders showed the highest mortality over T1D duration and neoplasms showed the lowest mortality (Figure 4.6).

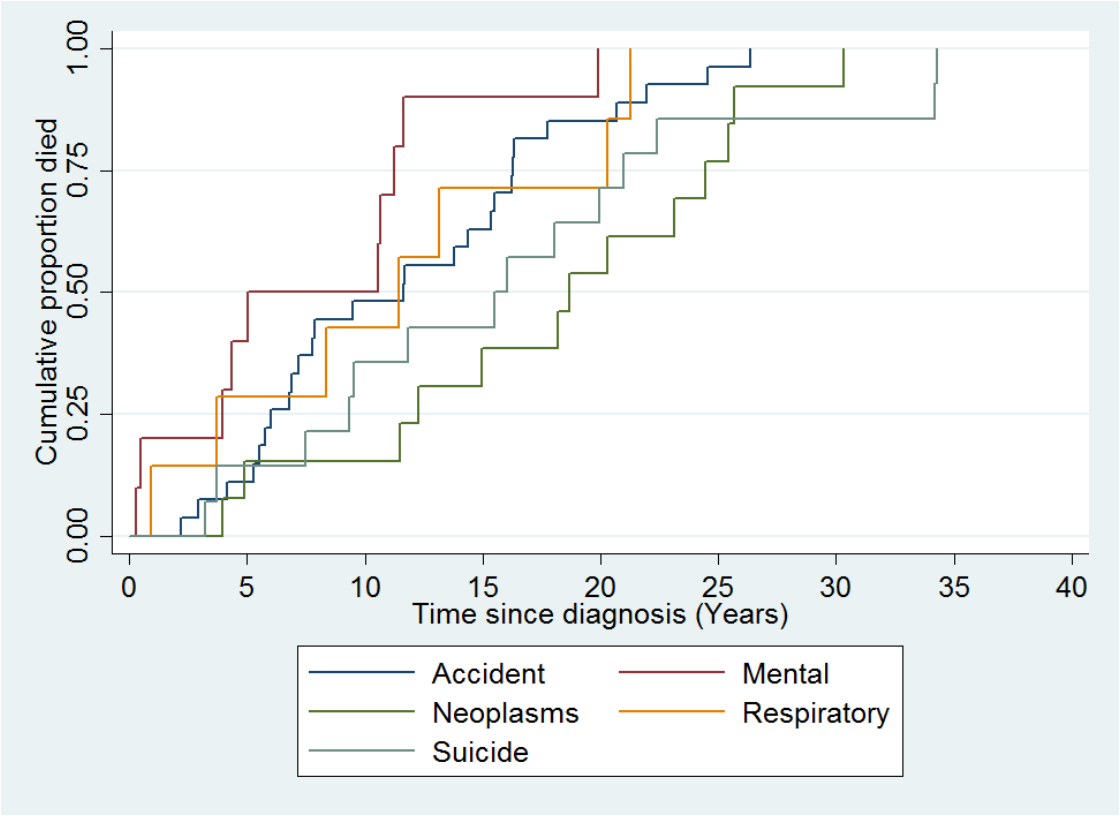


Figure 4.6: Cumulative mortality curves by non-type 1 diabetes (T1D) related underlying causes of death.

4.3.3.3 Standardised mortality ratios (SMRs).

Compared with the general population, the overall SMR for all-cause mortality found a significant excess of deaths in the YRDCYP of 4.3 (95% CI 3.8 to 4.9). SMRs for non-T1D related underlying cause of death found a significant excess of death compared with the general population for respiratory failure, mental disorder and suicide. There was no significant excess of deaths due to neoplasms and accidents and violence. The SMR for deaths due to mental disorder was significantly higher than the SMR for neoplasms (Figure 4.7).

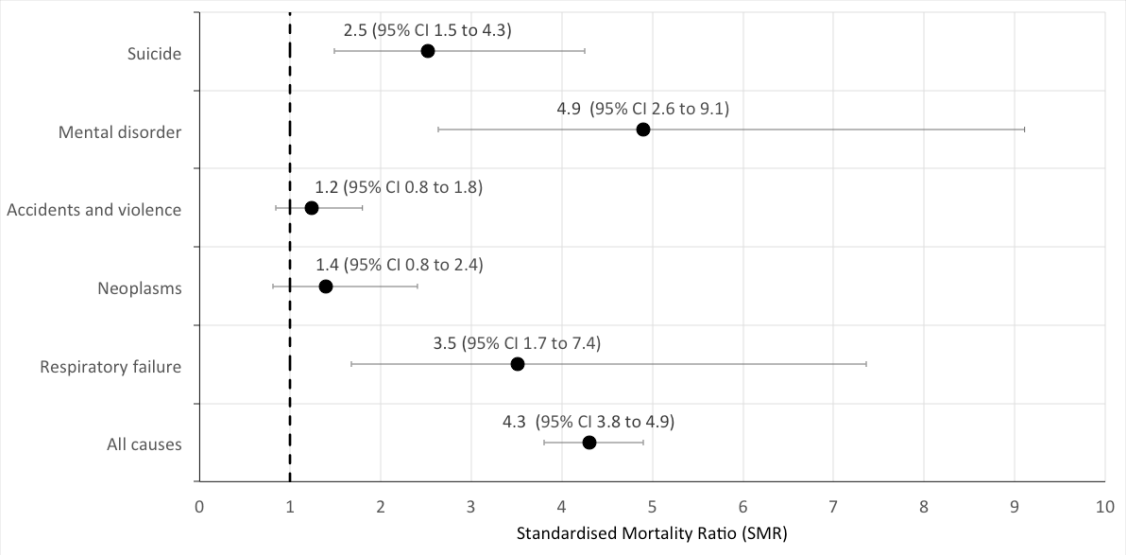


Figure 4.7: Standardised mortality ratios (SMRs) by all-cause mortality and non-type 1 diabetes (T1D) related deaths.

4.3.4 Mortality analysis of the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort by age at death.

There were 9 deaths before the transitional care period (under 15 years). A third of these deaths were due to DKA. There were no deaths due to severe hypoglycaemia or chronic T1D complications in this age group (Table 4.5).

During the transitional care period, there were 108 deaths. Forty-seven per cent (n=51) of these deaths were due to T1D-related underlying causes and the rest were non-T1D related deaths. Of the 51 T1D-related deaths, 30 were due to acute complications, with over a third of deaths due to DKA in the 15 to 19-year age group. Deaths due to T1D-related chronic complications started in the 20 to 24-year age group (Table 4.5). For non-T1D related deaths, the majority of deaths for respiratory failure, accidents and violence and mental disorder occurred during the transitional care period. Total deaths due to accidents and violence and mental disorder peaked within the 25 to 29-year old age group. The age group with the greatest total of deaths due to respiratory failure occurred in the 20 to 24-year age group (Table 4.6).

After the transitional care period, there were 112 deaths. Nearly 60% of these deaths were due to T1D-related underlying causes, with most deaths due to severe hypoglycaemia. Most T1D-related deaths due to renal and circulatory complications occurred after the transitional care period. Total deaths due to severe hypoglycaemia and renal complications peaked within the 35 to 39-year age group (Table 4.5). For non-T1D related deaths, most deaths due to neoplasms and suicide also occurred after the transitional care period. The 5-

year age groups with the greatest total of deaths for these causes occurred in the 40 to 44-year age group for neoplasms and 35 to 39 for suicide (Table 4.6).

4.3.4.1 Mortality rates.

Mortality rates for all-cause mortality by age at death showed a significantly lower mortality incidence rate for the 40 to 44 and the 45 to 49-year age groups compared with the overall all-cause mortality rate (Figure 4.8).

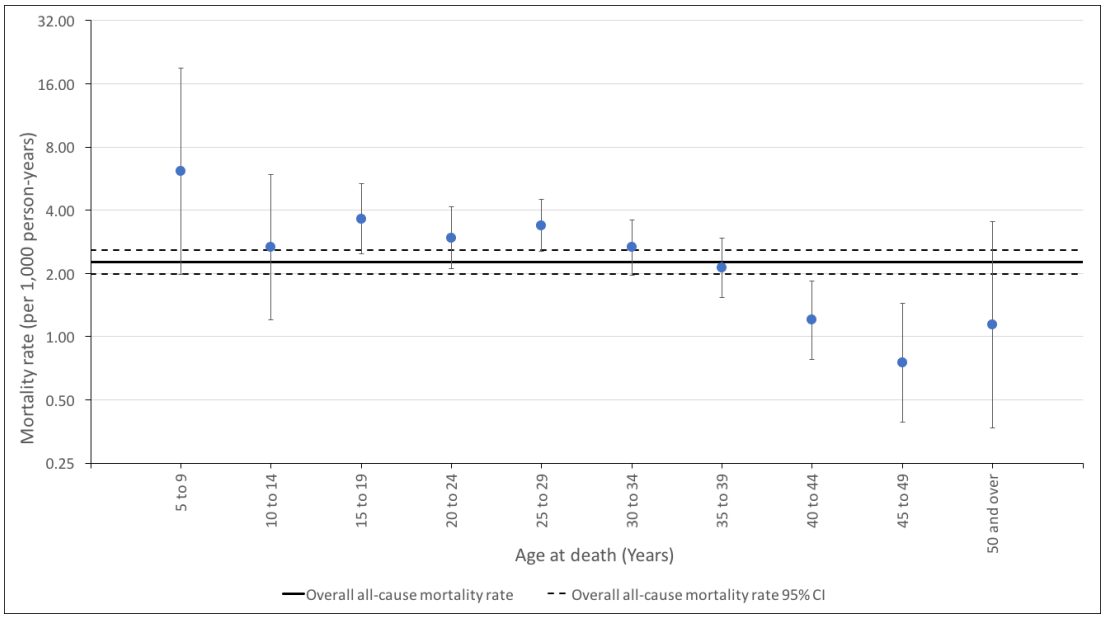


Figure 4.8: Mortality rates for all-cause mortality by age at death.

When comparing cause-specific mortality incidence rates by age at death, the 15 to 19-year age group have a significantly higher mortality incidence for DKA compared with the overall DKA mortality incidence rate (Figure 4.9; Table 4.9).

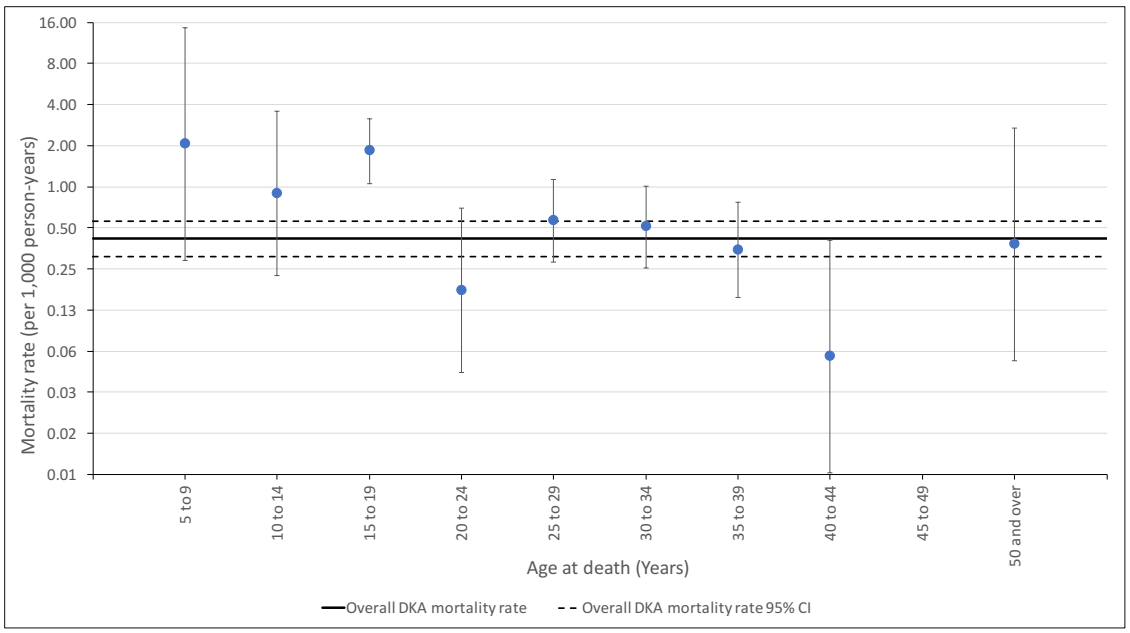


Figure 4.9: Mortality rates for type 1 diabetes (T1D) related deaths due to diabetic ketoacidosis (DKA) by age at death.

There were no other significant differences from the overall mortality rate for any T1D-related underlying cause of death (Table 4.9).

For all non-T1D related deaths, the 45 to 49-year age group had a significantly lower mortality rate compared with the overall non-T1D related mortality rate. For deaths due to neoplasms, the 5 to 9-year age group showed a significantly higher mortality rate compared with the overall neoplasm mortality rate for all ages. There were no other significantly different mortality rates by age groups compared with the overall cause-specific mortality rates for any other non-T1D related underlying causes of death (Table 4.10).

Table 4.9: Mortality rates (and 95% CI) per 10,000 person-years for all deaths and for type 1 diabetes (T1D) related deaths by age at death.

Age at death	All deaths	Type 1 diabetes-related deaths				
		All T1D deaths	DKA	Severe hypoglycaemia	Renal	Circulatory
5 to 9	6.13 (1.98 to 19)	2.04 (0.29 to 14.5)	2.04 (0.29 to 14.5)	-	-	-
10 to 14	2.66 (1.2 to 5.93)	0.89 (0.22 to 3.55)	0.89 (0.22 to 3.55)	-	-	-
15 to 19	3.64 (2.48 to 5.35)	**2.38** ** **(1.48 to 3.83)**	**1.82** ** **(1.06 to 3.13)**	-	-	-
20 to 24	2.96 (2.11 to 4.14)	1.13 (0.66 to 1.95)	0.17 (0.04 to 0.7)	0.35 (0.13 to 0.93)	0.09 (0.01 to 0.62)	0.17 (0.04 to 0.7)
25 to 29	3.39 (2.55 to 4.49)	1.48 (0.97 to 2.27)	0.56 (0.28 to 1.13)	0.28 (0.11 to 0.75)	0.21 (0.07 to 0.66)	0.14 (0.04 to 0.56)
30 to 34	2.66 (1.97 to 3.6)	1.39 (0.92 to 2.12)	0.51 (0.25 to 1.01)	0.06 (0.01 to 0.45)	0.13 (0.03 to 0.51)	0.19 (0.06 to 0.59)
35 to 39	2.13 (1.54 to 2.93)	1.38 (0.92 to 2.06)	0.34 (0.15 to 0.77)	0.06 (0.01 to 0.41)	0.46 (0.23 to 0.92)	0.23 (0.09 to 0.61)
40 to 44	**1.2*** **(0.78 to 1.84)**	0.63 (0.35 to 1.13)	0.06 (0.01 to 0.4)	0.23 (0.09 to 0.61)	0.06 (0.01 to 0.4)	0.17 (0.06 to 0.53)
45 to 49	**0.75*** **(0.39 to 1.44)**	0.5 (0.22 to 1.11)	-	-	0.08 (0.01 to 0.59)	0.17 (0.04 to 0.67)
50 and over	1.14 (0.37 to 3.52)	0.76 (0.19 to 3.03)	0.38 (0.05 to 2.69)	-	-	0.38 (0.05 to 2.69)
All ages	2.27 (1.99 to 2.58)	1.18 (0.98 to 1.41)	0.42 (0.31 to 0.56)	0.14 (0.08 to 0.23)	0.16 (0.1 to 0.26)	0.17 (0.1 to 0.27)

*Statistically significantly lower than the mortality rate for all ages.
**Statistically significantly higher than the mortality rate for all ages.

Table 4.10: Mortality rates (and 95% CI) per 10,000 person-years for non-type 1 diabetes (T1D) related deaths by age at death.

Age at death	Non-T1D related deaths					
	All deaths	**Respiratory failure**	**Neoplasms**	**Accidents and violence**	**Mental disorder**	**Suicide**
5 to 9	4.09 (1.02 to 16.34)	-	**2.04** (0.29 to 14.5)**	-	-	-
10 to 14	1.78 (0.67 to 4.73)	-	0.44 (0.06 to 3.15)	0.89 (0.22 to 3.55)	-	-
15 to 19	1.26 (0.66 to 2.42)	0.14 (0.02 to 0.99)	-	0.7 (0.29 to 1.68)	-	0.14 (0.02 to 0.99)
20 to 24	1.83 (1.19 to 2.8)	0.35 (0.13 to 0.93)	-	0.52 (0.23 to 1.16)	0.17 (0.04 to 0.7)	0.26 (0.08 to 0.81)
25 to 29	1.9 (1.31 to 2.78)	-	0.21 (0.07 to 0.66)	0.56 (0.28 to 1.13)	0.42 (0.19 to 0.94)	0.14 (0.04 to 0.56)
30 to 34	1.27 (0.82 to 1.96)	0.13 (0.03 to 0.51)	0.13 (0.03 to 0.51)	0.25 (0.1 to 0.67)	0.13 (0.03 to 0.51)	0.13 (0.03 to 0.51)
35 to 39	0.75 (0.43 to 1.29)	-	0.06 (0.01 to 0.41)	0.06 (0.01 to 0.41)	-	0.23 (0.09 to 0.61)
40 to 44	0.57 (0.31 to 1.06)	-	0.23 (0.09 to 0.61)	0.06 (0.01 to 0.4)	-	0.11 (0.03 to 0.46)
45 to 49	**0.25* (0.08 to 0.77)**	-	0.08 (0.01 to 0.59)	-	-	-
50 and over	0.38 (0.05 to 2.69)	-	-	-	-	-
All ages	1.09 (0.9 to 1.31)	0.07 (0.03 to 0.15)	0.13 (0.07 to 0.22)	0.27 (0.18 to 0.39)	0.1 (0.05 to 0.18)	0.14 (0.08 to 0.23)

*Statistically significantly lower than the mortality rate for all ages.
**Statistically significantly higher than the mortality rate for all ages.

4.3.4.2 Standardised mortality ratios (SMRs).

SMRs by age at death showed significant excess of deaths compared with the general population from the 10 to 14-year age group onwards (Figure 4.11). Although there are no significant differences in SMRs between age groups, there appeared to be an increasing trend in SMRs up to 5.9 (95% CI 4.4 to 7.8) in the 25 to 29-year age group. SMRs then began to decrease gradually for the older age groups. The 50 and over age group had the highest SMR at 6.7 (95% CI 2.1 to 20.7). However, there were only three deaths in this age group (Table 4.5).

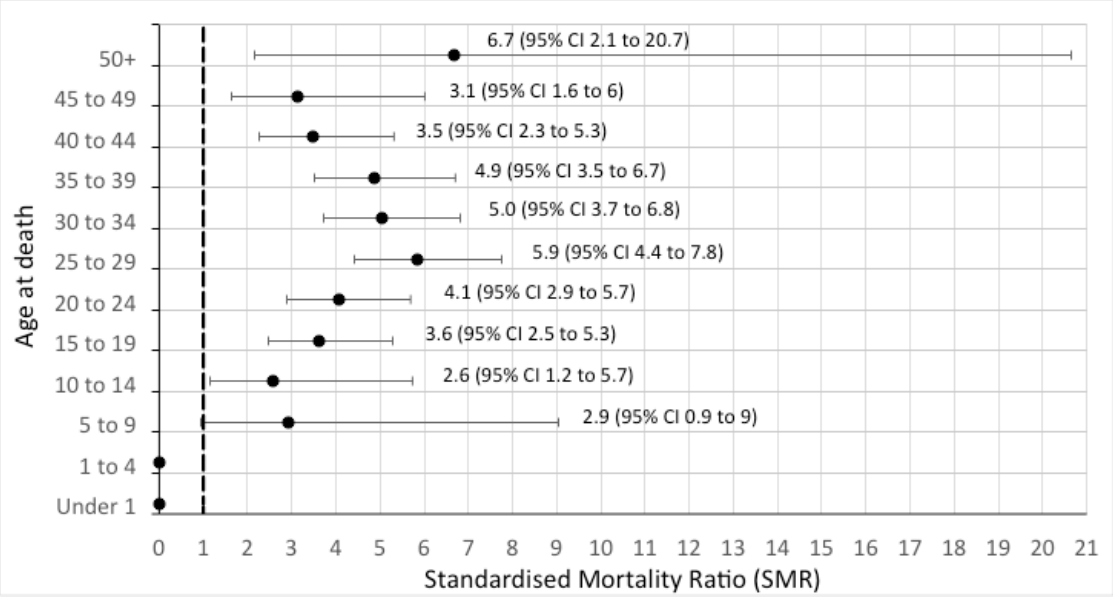


Figure 4.10: Standardised mortality ratios (SMRs) by age at death.

4.3.5 Mortality analysis of the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort by age of T1D onset group.

There were more deaths in the group diagnosed with early T1D onset (n=156) compared with the group diagnosed with late T1D onset (n=73) (Table 4.5). However, the percentage of deaths in the late T1D onset group (6.5%) was nearly twice the percentage of deaths in the early T1D onset group (3.6%).

The percentage of deaths due to all T1D-related underlying causes was greater in the early T1D onset group at 56.4% compared with the late T1D onset group at 42.5%. The early T1D onset also had a greater percentage of deaths compared with the late T1D onset group for deaths due to DKA and severe hypoglycaemia. For T1D-related deaths due to chronic complications, the percentage of deaths due to renal complications was similar between the onset

groups. However, the percentage of deaths due to circulatory complications in the early T1D onset group was around 3.5 times that of the late T1D onset group (Table 4.5).

For non-T1D related deaths, the late T1D onset group had a higher percentage of deaths due to neoplasms, mental disorder and suicide (Table 4.6).

4.3.5.1 Mortality rates.

There was a significantly higher all-cause mortality rate for the late T1D onset group compared with both the all-cause mortality rate for the whole cohort and for the all-cause mortality incidence rate for the early T1D onset group. When examining cause-specific mortality, only deaths due to non-T1D related causes had a significantly higher mortality rate for the late T1D onset group compared with the whole cohort and the early T1D onset group (Table 4.7).

4.3.5.2 Survival analysis.

Cumulative mortality curves by onset group show higher mortality over T1D duration for the early T1D onset group compared with the late T1D onset group (Figure 4.11).

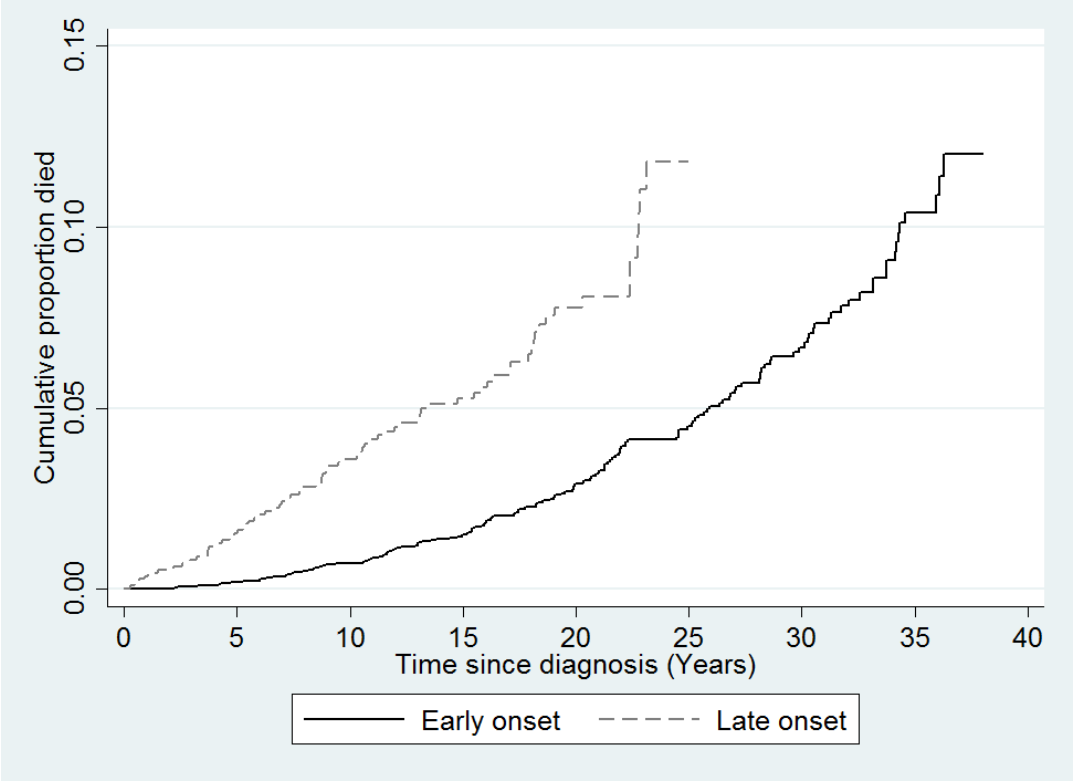


Figure 4.11: Cumulative mortality curves by age at type 1 diabetes (T1D) onset group.

Log-rank test found that there was a statistically significant difference in cumulative mortality between the onset groups (Table 4.11).

Table 4.11: Log-rank tests for Kaplan-Meier estimators by socio-demographic group 1 and socio-demographic group 2.

Socio-demographic group 1	Socio-demographic group 2	p-value
Early T1D onset	Late T1D onset	**<0.00***
Males	Females	**<0.00***
White	South Asian	**0.02***
Least deprived fifth	2nd least deprived fifth	0.85
Least deprived fifth	3rd most deprived fifth	0.51
Least deprived fifth	2nd most deprived fifth	0.28
Least deprived fifth	Most deprived fifth	0.28
2nd least deprived fifth	3rd most deprived fifth	0.60
2nd least deprived fifth	2nd most deprived fifth	0.34
2nd least deprived fifth	Most deprived fifth	0.33
3rd most deprived fifth	2nd most deprived fifth	0.61
3rd most deprived fifth	Most deprived fifth	0.65
2nd most deprived fifth	Most deprived fifth	0.95

*Statistically significant difference in cumulative mortality between socio-demographic group 1 and socio-demographic group 2.

Cox regression modelling found that late T1D onset had over a three-fold significantly higher risk of all-cause mortality compared with early T1D onset, when adjusted for sex, year of diagnosis and deprivation (Table 4.12). Separate analysis of both early and late onset groups showed that those diagnosed in later years had a significantly lower risk of all-cause mortality, where for each one year increase in year of diagnosis the HR was 0.97 (95% CI 0.94 to 0.99) and 0.93 (95% CI 0.88 to 0.99), respectively (Table 4.12).

For all T1D-related mortality, Cox regression modelling found that the late onset group had a significantly higher risk of death compared with the early onset group (Table 4.13). However, no significant differences between the onset groups were found for acute complications, DKA or severe hypoglycaemia. There was a significantly higher HR for deaths due to T1D-related chronic complications for the late onset group compared with the early onset group by over six-fold.

For non-T1D related mortality, Cox regression modelling found significantly higher HRs for the late onset group compared with the early onset group for all non-T1D related deaths and deaths due to neoplasms, accidents and violence, mental disorder and suicide (Table 4.14).

Table 4.12: Cox regression hazard ratios (and 95% CI) by age at type 1 diabetes (T1D) onset group for all-cause mortality.

Age at T1D diagnosis	Late onset vs early onset	Females vs males	Year of diagnosis	Most deprived fifth vs least deprived fifth	2nd most deprived fifth vs least deprived fifth	3rd most deprived fifth vs least deprived fifth	2nd least deprived fifth vs least deprived fifth
All	**3.69 (2.63 to 5.16)****	**0.45 (0.34 to 0.61)***	**0.96 (0.94 to 0.98)***	1.47 (0.93 to 2.33)	1.55 (0.97 to 2.49)	1.36 (0.84 to 2.21)	1.15 (0.68 to 1.93)
0 to 14 years (early onset)	-	**0.46 (0.33 to 0.65)***	**0.97 (0.94 to 0.99)***	1.32 (0.75 to 2.33)	1.36 (0.76 to 2.44)	1.15 (0.63 to 2.09)	1.01 (0.53 to 1.93)
15 to 29 years (late onset)	-	**0.44 (0.25 to 0.76)***	**0.93 (0.88 to 0.99)***	1.72 (0.78 to 3.77)	1.9 (0.85 to 4.26)	1.86 (0.82 to 4.27)	1.41 (0.59 to 3.35)

*Statistically significantly lower hazard ratio.
**Statistically significantly higher hazard ratio.

Table 4.13: Cox regression hazard ratios (and 95% CI) by age at type 1 diabetes (T1D) onset group for T1D-related mortality.

Underlying cause of death	Age at T1D diagnosis	Late onset vs early onset	Females vs males	Year of diagnosis	Most deprived fifth vs least deprived fifth	2nd most deprived fifth vs least deprived fifth	3rd most deprived fifth vs least deprived fifth	2nd least deprived fifth vs least deprived fifth
All T1D-related deaths	All	**3.05 (1.86 to 5)****	**0.49 (0.33 to 0.73)***	**0.96 (0.93 to 0.995)***	1.21 (0.63 to 2.32)	1.7 (0.89 to 3.25)	1.45 (0.74 to 2.81)	1.05 (0.5 to 2.18)
	0 to 14 years (early onset)	-	**0.48 (0.31 to 0.75)***	**0.96 (0.93 to 0.999)***	0.81 (0.39 to 1.69)	1.24 (0.61 to 2.53)	1.1 (0.53 to 2.28)	0.84 (0.37 to 1.91)
	15 to 29 years (late onset)	-	0.53 (0.24 to 1.19)	0.96 (0.88 to 1.05)	3.8 (0.83 to 17.37)	4.47 (0.96 to 20.68)	3.3 (0.66 to 16.36)	2.12 (0.39 to 11.57)
T1D-related deaths due to acute complications	All	1.81 (0.91 to 3.62)	**0.55 (0.31 to 0.96)***	0.99 (0.95 to 1.03)	0.94 (0.37 to 2.35)	1.35 (0.55 to 3.32)	1.25 (0.5 to 3.14)	1.25 (0.5 to 3.14)
	0 to 14 years (early onset)	-	**0.51 (0.27 to 0.96)***	0.99 (0.94 to 1.03)	0.65 (0.23 to 1.83)	1.08 (0.41 to 2.88)	1.05 (0.39 to 2.83)	0.63 (0.19 to 2.08)
	15 to 29 years (late onset)	-	0.68 (0.2 to 2.17)	1.05 (0.92 to 1.19)	3.07 (0.34 to 27.5)	2.86 (0.3 to 27.52)	2.09 (0.19 to 23.08)	3.22 (0.33 to 31)
T1D-related deaths due to acute complications (DKA)	All	1.85 (0.87 to 3.92)	0.52 (0.27 to 1.01)	1.01 (0.96 to 1.06)	1.4 (0.44 to 4.42)	1.58 (0.49 to 5.06)	1.71 (0.54 to 5.49)	1.48 (0.43 to 5.05)
T1D-related deaths due to acute complications (severe hypoglycaemia)	All	1.8 (0.31 to 10.49)	0.61 (0.2 to 1.82)	0.93 (0.84 to 1.02)	0.33 (0.05 to 1.96)	1.04 (0.25 to 4.4)	0.64 (0.13 to 3.17)	0.27 (0.03 to 2.64)
T1D-related deaths due to chronic complications	All	**6.26 (2.25 to 17.46)****	0.64 (0.34 to 1.2)	**0.9 (0.84 to 0.97)***	1.32 (0.41 to 4.23)	2.26 (0.73 to 6.96)	1.74 (0.54 to 5.58)	1.27 (0.36 to 4.51)
	0 to 14 years (early onset)	-	0.56 (0.27 to 1.14)	0.89 (0.82 to 0.97)	0.69 (0.19 to 2.44)	1.5 (0.47 to 4.79)	1.01 (0.3 to 3.46)	1.18 (0.33 to 4.18)
	15 to 29 years (late onset)	-	1.04 (0.29 to 3.69)	0.93 (0.76 to 1.13)	-	-	-	-

*Statistically significantly lower hazard ratio.
**Statistically significantly higher hazard ratio.

Table 4.14: Cox regression hazard ratios (and 95% CI) for non-type 1 diabetes (T1D) related mortality.

Underlying cause of death	Age at T1D diagnosis	Late onset vs early onset	Females vs males	Year of diagnosis	Most deprived fifth vs least deprived fifth	2nd most deprived fifth vs least deprived fifth	3rd most deprived fifth vs least deprived fifth	2nd least deprived fifth vs least deprived fifth
All non-T1D related deaths	All	**4.35 (2.74 to 6.91)**	**0.41 (0.27 to 0.63)**	**0.96 (0.93 to 0.99)**	1.78 (0.93 to 3.4)	1.37 (0.68 to 2.76)	1.25 (0.61 to 2.57)	1.26 (0.6 to 2.64)
	0 to 14 years (early onset)	-	**0.44 (0.26 to 0.74)**	0.97 (0.94 to 1.01)	2.45 (0.94 to 6.34)	1.64 (0.6 to 4.52)	1.25 (0.44 to 3.61)	1.38 (0.46 to 4.11)
	15 to 29 years (late onset)	-	**0.37 (0.17 to 0.8)**	**0.91 (0.85 to 0.99)**	1.12 (0.43 to 2.94)	1.16 (0.42 to 3.19)	1.46 (0.54 to 3.92)	1.21 (0.44 to 3.34)
Neoplasms	All	**14.27 (2.63 to 77.54)****	0.55 (0.17 to 1.78)	0.92 (0.81 to 1.05)	1.49 (0.29 to 7.74)	0.78 (0.11 to 5.59)	0.81 (0.11 to 5.84)	0.91 (0.13 to 6.44)
Accidents and violence	All	**3.57 (1.37 to 9.29)****	0.5 (0.22 to 1.15)	**0.92 (0.87 to 0.98)***	1.79 (0.49 to 6.55)	0.91 (0.2 to 4.1)	0.96 (0.21 to 4.32)	1.74 (0.43 to 6.96)
Mental disorder	All	**13.6 (2.79 to 66.41)****	0.59 (0.15 to 2.29)	0.94 (0.84 to 1.04)	2.61 (0.29 to 23.49)	0.82 (0.05 to 13.25)	2.71 (0.28 to 26.22)	0.96 (0.06 to 15.46)
Suicide	All	**4.21 (1.17 to 15.09)****	**0.09 (0.01 to 0.71)***	0.98 (0.89 to 1.08)	0.39 (0.06 to 2.36)	1 (0.22 to 4.5)	0.52 (0.09 to 3.12)	0.91 (0.18 to 4.54)

*Statistically significantly lower hazard ratio.
**Statistically significantly higher hazard ratio.

4.3.5.3 Standardised mortality ratios (SMRs).

Despite differences found between the early and late T1D onset groups for all-cause mortality incidence rates and Cox regression modelling, there were no significant differences in SMRs between the onset groups. The SMRs were 4.1 (95% CI 3.6 to 4.8) for the early T1D onset group and 4.7 (95% CI 3.8 to 5.9) for the late T1D onset group.

For T1D-related underlying causes of death, there were 16 deaths due to IHD with an SMR of 8.5 (95% CI 5.2 to 13.9). In early onset, there were 14 deaths, beginning in the 20 to 24-0year age group, with a median age at death of 35.1 years and SMR of 13.8 (95% CI 8.2 to 23.3). There was no significant excess in deaths due to IHD in the late onset group (SMR 2.3 (95% CI 0.6 to 9.3)) where there were 2 deaths (both male) which occurred in the 35 to 39 and the 50 and over age group.

Suicide was the only non-T1D related underlying cause of death where there was an excess in deaths for both early (SMR 2.1 (95% CI 1.0 to 4.2)) and late T1D onset (SMR 3.5 (95% CI 1.6 to 7.7)).

4.3.6 Mortality analysis of the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort by sex.

The percentage of deaths in males was higher at 7.2% compared with the percentage of deaths in females which was 3.0%.

The percentage of deaths due to all T1D-related underlying causes was higher in the females (56.3%) compared with males (50.3%). Females had a slightly greater percentage of deaths compared with males for deaths due to DKA and severe hypoglycaemia. For T1D-related deaths due to chronic complications, the percentage of deaths due to circulatory complications was similar for both sexes. However, the percentage of deaths due to renal complications in females was around 3 times that of males (Table 4.5).

For non-T1D related deaths, the percentages of deaths for respiratory failure, neoplasms, accidents and violence and mental disorder were similar between the sexes. However, there were 7.9% of male deaths due to suicide, compared with 1.6% of female deaths due to suicide (Table 4.6).

4.3.6.1 Mortality rates.

All-cause mortality rate for males was significantly higher compared with the all-cause mortality rate for the whole cohort and for the all-cause mortality rate for females. The all-cause mortality rate for females was significantly lower than the all-cause mortality rate for the whole cohort (Table 4.7).

Cause-specific mortality rate found that T1D-related deaths was significantly different between the sexes, where males had a significantly higher mortality rate compared with females. There were no significant differences between the sexes for T1D-related deaths due to acute or chronic complications (Table 4.7) or for non-T1D related causes (Table 4.8).

4.3.6.2 Survival analysis.

Cumulative mortality curves by sex show a higher mortality over T1D duration for males compared with females (Figure 4.12). The log-rank test found that there was a statistically significant difference in cumulative mortality between the sexes (Table 4.11).

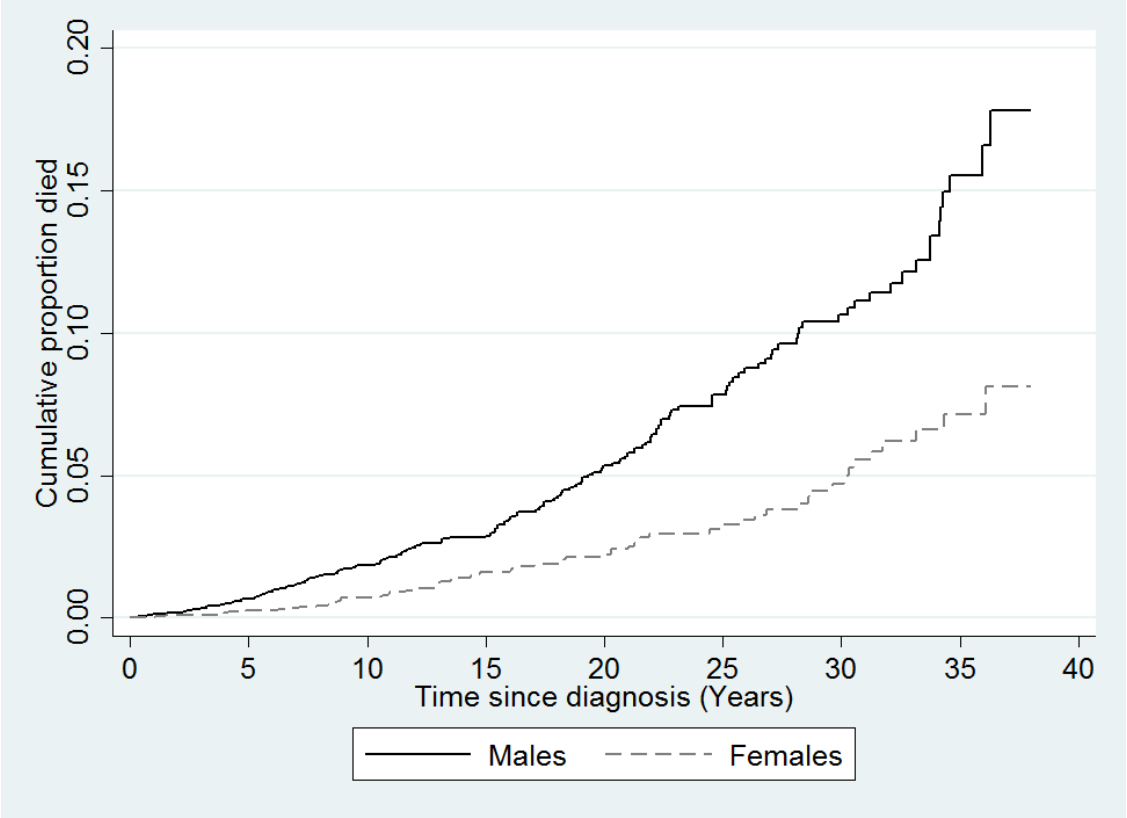


Figure 4.12: Cumulative mortality curves by sex.

Cox regression modelling found that females had a lower mortality risk from all-cause mortality (Table 4.12), T1D-related (Table 4.13), all non-T1D related deaths and suicide (Table 4.14). Females also had lower mortality risk in the early T1D onset only for all-cause (Table 4.12), T1D-related mortality (Table 4.13). Both early and late onset groups had significantly lower risk of death for females compared with males for all non-T1D related mortality (Table 4.14). However, there were no significant differences in mortality risk between males and females by T1D-related acute (including DKA and severe hypoglycaemia) or chronic complications (Table 4.13).

4.3.6.3 Standardised mortality ratios (SMRs).

Although most deaths occurred in males, the SMR for males (4.4 (95% CI 3.8 to 5.2); n=165) was similar to females (4.0 (95% CI 3.2 to 5.2); n=64).

Mental disorder deaths were significantly higher for males (SMR 4.2 (95% CI 2.0 to 8.7) and females 8.4 (SMR 95% CI 2.7 to 26.03) compared with the general population. Males only had a significant excess in deaths for suicide (SMR 2.8 (95% CI 1.6 to 4.8)) and respiratory failure (SMR 4.1 (95% CI 1.7 to 9.8)).

4.3.7 Mortality analysis of the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort by ethnicity.

The percentage of deaths for white ethnic origin was higher at 5.1% compared with the percentage of deaths for South Asian origin which was 3%. There were no deaths for the ‘Other’ ethnicity group.

The percentage of deaths due to all T1D-related underlying causes was 50.3% in the white ethnicity group compared with 22.2% in the South Asian ethnicity group. There were no T1D-related deaths due to acute complications for South Asian ethnicity and there was only one T1D-related death due to renal complications for South Asian ethnicity (Table 4.5).

4.3.7.1 Survival analysis.

The cumulative mortality curves between white and South Asian ethnicity showed higher mortality for the white ethnic origin group (Figure 4.13). The log-rank test found a statistically significant difference between cumulative mortality curves between white and South Asian ethnicity (Table 4.11).

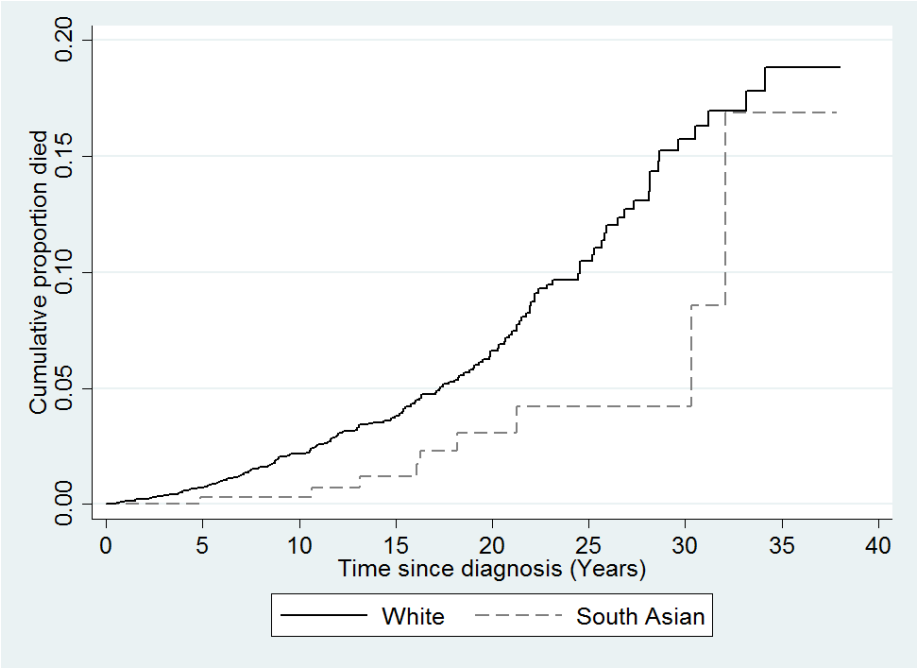


Figure 4.13: Cumulative mortality curves by ethnicity.

4.3.7.2 Standardised mortality ratios (SMRs).

Both white and South Asian ethnicity had a significant excess in mortality compared with the general population. However, the SMR was significantly higher for white ethnicity compared to South Asian (8.1 (95% CI 6.9 to 9.4) vs. 3.4 (95% CI 1.7 to 6.4)).

White ethnicity had an excess in mental health-related mortality (12.9 (95% CI 6.7 to 24.8)) and exhibited an excess of deaths due to accidents (2.8 (95% CI 1.8 to 4.1)). South Asian ethnicity had an excess in deaths due to neoplasms (SMR 6.5 (95% CI 2.1 to 20.1).

4.3.8 Mortality analysis of the Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort by deprivation group.

The percentage of deaths is similar between each deprivation group at around 5%. The highest percentage was found in the most deprived fifth at 5.4% and the lowest percentage was found in the 2nd least deprived fifth at 4.9% (Table 4.4).

4.3.8.1 Mortality rates.

The most deprived fifth had the highest all-cause mortality rate of the five deprivation groups and the least deprived fifth had the lowest mortality rate. However, there were no significant differences in mortality rates between any of the deprivation groups. Mortality rates by cause-specific mortality also found no significant differences by deprivation groups (Table 4.7, Table 4.8).

4.3.8.2 Survival analysis.

Cumulative mortality curves show higher mortality in the most deprived fifth compared with the least deprived fifth from around 10 years T1D duration, particularly during 20 to around 34 years since T1D diagnosis (Figure 4.14). However, log-rank tests showed that there was no significant difference between these two groups. Log rank tests were performed between all other deprivation groups and no other significant difference in mortality over T1D duration was found between any other deprivation groups (Table 4.11).

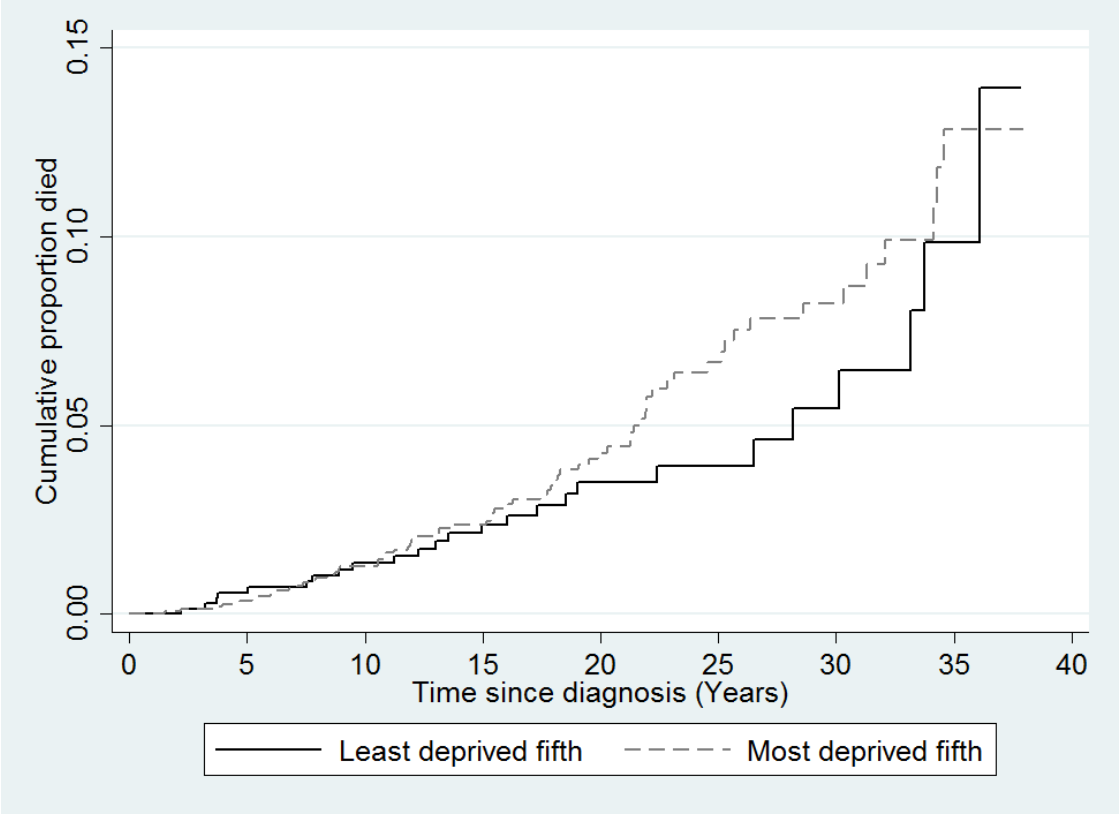


Figure 4.14: Cumulative mortality curves by deprivation groups.

Cox regression modelling found no significant difference in mortality risk between each of the four most deprived fifths and the least deprived fifth for

overall all-cause, T1D-related and non-T1D related mortality. There were no other significant differences by deprivation by onset group and underlying cause (Table 4.13).

4.3.8.3 Standardised mortality ratios (SMRs).

All deprivation categories had an excess of deaths compared to the general population. Although there is a slight visible decreasing trend in SMRs from the most deprived fifth to the least deprived fifth, there were no significant differences found in SMRs between any of the deprivation groups (Figure 4.15).

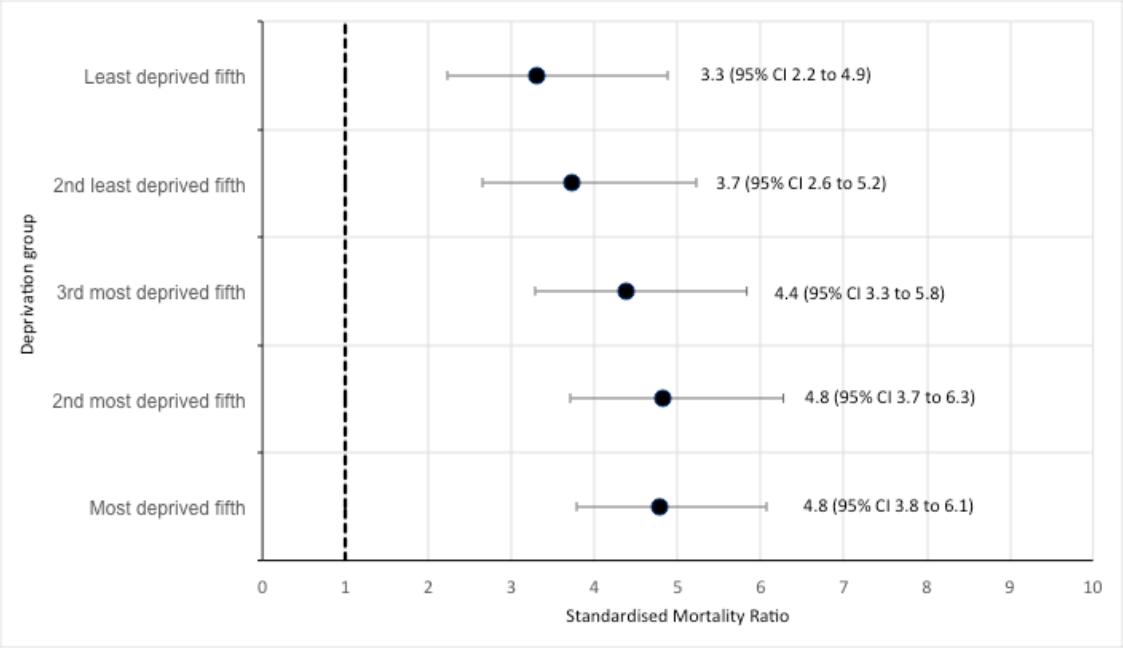


Figure 4.15: Standardised mortality ratios (SMRs) for all-cause mortality by deprivation group.

4.3.9 Cox regression modelling diagnostics.

The test for proportional hazards assumptions for the Cox regression models found no evidence that the proportional hazards assumption had been violated (Table 4.15).

Table 4.15: Global test results for proportional hazards assumption.

Underlying cause of death	Global test for proportional hazards assumption
All causes	0.5138
	0.1999
	0.7137
T1D-related deaths	0.6916
	0.4715
	0.9133
Non-T1D related deaths	0.6731
	0.4793
	0.8549

4.4 Summary of results.

Analysis by age at death showed some evidence for more deaths during the transitional care period. T1D-related deaths due to DKA had a significantly higher mortality rate in the 15 to 19-year age group compared with the over 40 DKA mortality rate. However, T1D-related deaths due to severe hypoglycaemia, renal and circulatory complications mostly appeared after the transitional age group.

Analysis by age at T1D onset groups found significantly higher mortality in the late onset group. Cox regression models found statistically significantly higher mortality in the late onset group for all-cause, T1D-related and non-T1D related mortality. There was, however, a significant excess in deaths due to IHD in early onset which was not found in the late onset group.

Males were shown to have significantly higher mortality compared with females for all-cause and T1D-related mortality. For non-T1D related deaths, males had a higher percentage of deaths due to suicide compared with females. There was also an excess of deaths by suicide compared with the general population in males but not females.

There was significantly higher mortality in the white ethnic origin group compared with South Asian ethnicity, although there was a large percentage of the cohort where ethnicity could not be classified.

There was no evidence of any significant differences in all-cause or cause-specific mortality by deprivation groups.

4.5 Overall summary analysis compared with previous studies.

The overall SMR (ratio between the observed and the expected number of deaths) for the YRDCYP (4.3; 95% CI 3.8 to 4.9) was similar to the SMR found on the previous analysis of the dataset (4.7; 95% CI 3.8 to 5.6), indicating an excess of deaths in the T1D population compared with the general population (175). An excess in deaths was also found across different countries in a review for 23 studies by Morgan and colleagues, where the SMR ranged between 0 to 8.54 (266). This review mostly included individuals with early T1D onset, so direct comparison of SMRs with these studies should be treated with caution. The only other cohort to include individuals diagnosed with both early and late T1D onset (under 30 years old) was in the New Zealand Canterbury Diabetes Registry; Brown and colleagues found an overall SMR of 2.64 (95% CI 2.36 to 2.96), around half the excess number of deaths compared with this analysis (267). The YRDCYP cohort included a larger number of individuals (n=5,498) compared with the Canterbury cohort (n=1,008) and covered a longer follow-up period (9 years vs. 35 years), which may explain the difference in SMRs between the two datasets.

4.6 Health outcomes by attained age groups before, during and after the transitional care period.

There are few previous studies to have included SMRs by age, particularly comparing time periods before, during and after the transitional care period. For all-cause mortality in the YRDCYP, there was a non-significant trend of increasing SMRs with age at death. There was a peak during the transitional care period, with the highest SMR in the 25 to 29 age group (5.9 (95% CI 4.4 to 7.8)), before decreasing after the transitional care period. This trend was similar to results by Brown and colleagues in the New Zealand Canterbury Diabetes Registry, although the peak SMR occurred in the 30 to 39-year age group at 9.23 (95% CI 4.77 to 16.15), before decreasing with older age groups (267). There was no age breakdown in the Canterbury cohort before and during the transitional care period. Dahlquist and Kallen (2005) did include age groups before and after the transitional care period and found that the highest SMR occurred in the 10 to 14-year age group (SMR (4.38 (95% CI 1.14 to 4.37)) (192). However, this Swedish cohort only included individuals with early onset T1D.

For T1D-related mortality, analysis by age at death in the YRDCYP showed some evidence for more deaths during the transitional care period compared

with other age groups. The 15 to 19-year age group was the only age group to have a significantly higher overall T1D-related and DKA mortality rates compared with the overall mortality rate for all ages.

4.7 Health outcomes by onset before and during the transitional care period.

There was no significant difference in SMRs between early (0 to 14 years) and late T1D onset (15 to 29 years) for all-cause mortality. Survival analysis showed there was a significantly higher all-cause mortality risk in the late onset group up to 20 years of diabetes duration. As the late onset group were older than the early onset group, early death observed in early onset could be due to longer duration of T1D, allowing for risk factors of mortality to develop at an earlier age. Previous research has seen similar findings with all-cause mortality where pre-pubertal groups (diagnosed before 12 in males and before 11 in females) have lower mortality risk than in pubertal groups (diagnosed between 12 and 16 in males and 11 and 16 in females) (268,269). In those diagnosed in older ages (30 years and over), Florkowski (2003) found a decreasing excess mortality with increasing age at T1D diagnosis and duration of those diagnosed with T1D under 30 and survived to 50 years of age had the same life expectancy as the general population (193).

For cause-specific mortality, the HR was significantly higher in the late T1D onset group for chronic T1D-related complications and deaths due to mental health disorder and suicide. An explanation for these differences between onset groups could be due to the difference in experience and knowledge of managing T1D. For example, a child diagnosed with T1D may have had more preparation in managing T1D through the transitional care period compared with someone diagnosed during the transitional care period. Gibb and colleagues found some evidence for this where they also found a higher risk of DKA mortality and recurrent DKA hospitalisations in those diagnosed in adolescence compared with those diagnosed as children (270).

4.8 Health outcomes by socio-demographic groups.

No significant differences were found in all-cause SMRs between sexes. The New Zealand Canterbury cohort (193,267) and a multi-centre Danish cohort (196) also found no significant differences in all-cause SMRs between males and females. However, other studies have shown a significantly higher SMR for

females compared with males in Japan and Finland (176,271), Australia (186), Sweden (192) and Italy (197). This may be due to differences between countries in mortality rates in the general population. For example, in 2016 the adult mortality rate for 15 to 60-year olds in the UK for females was 52 per 1,000 population. In Japan, the mortality rate was lower at 36 per 1,000 population (263). An excess in deaths in the T1D population may appear larger for females in Japan when the mortality rate in the general population is low.

For cause-specific mortality, sex differences were found for both T1D and non-T1D related deaths. Cox regression found that only sex was significantly associated with mortality risk from T1D acute complications, with a notable increased risk in males. However, it was difficult to ascertain whether deaths due to acute complications were self-inflicted with the intention of suicide. This could mean that suicide rates were underestimated. The number of suicides was highest in males with nearly 10% of all male deaths due to suicide. Higher suicide rates were also reported for males compared with females in Harjutsalo and colleagues' study in Finland and also in the DCCT cohort (172,176). The DCCT cohort also found nominally more suicides in the intensive treatment group compared with the conventional treatment group, suggesting that the introduction of intensive insulin treatment may be associated with an increase in mental health issues, although this link needs more examination (172).

Few UK studies have analysed mortality by ethnicity, possibly due to difficulties in collecting ethnicity data. However, there was evidence from the Allegheny cohort (USA) that excess deaths were associated with black ethnicity compared with white ethnicity due to diabetes complications (201,202). Ethnicity is often linked with deprivation, where minority ethnic groups are more likely to be most deprived. Collier and colleagues found no differences between African-Americans and white low socio-economic status Americans (173). White ethnicity had a significantly higher SMR compared with South Asians, contradicting international studies where minority ethnicities are associated with higher mortality risk (177,197,201). However, around 32% of the cohort had incomplete full names, so could not be classified to an ethnicity group by Onomap software. Additionally, Onomap had limitations in ability to consider marital status name changes and identification of mixed ethnicities. This could mean that the South Asian total could be underestimated.

There were no significant differences for all-cause or cause-specific SMRs by deprivation. Few studies have included analysis by deprivation. Where there has been analysis, having lower socio-economic status increased risk of death (186,197,198,270,272–275). However, it is difficult to compare results with other studies where different definitions of deprivation are used.

4.9 Chapter summary.

Analysis of mortality in a cohort of individuals with T1D showed some evidence of an increase of death during the transitional care period, with a peak in SMRs for all-cause mortality in the 25 to 29-year age group and a significantly higher rate of deaths due to DKA in the 15 to 19-year age group. DKA was further examined in the LCYPDS for individuals receiving CSII in chapter 5.

There was also evidence to suggest that there was a difference in mortality between age at T1D onset groups, where the late onset group had a significantly higher risk of death due to chronic T1D-related complications, mental health and suicide.

Analysis by socio-demographics found significant differences between sexes and ethnicity. There was an increased risk of death due to acute T1D-related in males compared with females. Males also had a higher percentage of deaths due to suicide. White ethnicity had a significantly higher SMR for all-cause mortality compared with South Asian ethnicity, in contrast to international studies where ethnic minority groups were found to have an increase in death.

Chapter 5 continues using a T1D cohort (LCYPDS) to examine negative health outcomes, focusing on individuals receiving CSII therapy. Although limited in follow-up time and age coverage, the LCYPDS cohort provided valuable insight into the patient pathway assessing hospitalisations and sex differences in negative health outcomes.

Chapter 5 Continuous Subcutaneous Insulin Infusion (CSII) therapy for type 1 diabetes (T1D).

This chapter describes the statistical methodology used and results from analysis of the LCYPDS dataset. It begins by defining the categorisations of the data and continues with a description of the statistics used in the analysis and reports the results.

There were two main health outcomes measured using the LCYPDS dataset:

1. HbA1c value since T1D diagnosis before and after CSII therapy initiation.
2. Hospitalisation rates since T1D diagnosis before and after CSII therapy initiation.

5.1 Variable definitions.

5.1.1 Pre-, during and after continuous subcutaneous insulin infusion (CSII) therapy time periods.

Details on categorising HbA1c values and hospitalisations between pre-, during and post-CSII are found in section 3.2.2.

5.1.2 Continuous subcutaneous insulin infusion (CSII) therapy status.

The CSII therapy status referred to whether an individual continued or discontinued CSII therapy whilst attending the LCYPDS. Any individual with a CSII therapy end date was classed as having discontinued CSII therapy. Individuals with no CSII end date were classed as having continued CSII therapy up to their last recorded appointment date. It could not be determined whether CSII therapy continued beyond that date.

5.1.3 Continuous subcutaneous insulin infusion (CSII) duration categorisation.

CSII duration was categorised by one year time periods. Further subgrouping was completed for the first year by ‘under 3 months’, ‘3 to under 6 months’ and ‘6 months to under 1 year’. This subgrouping was useful analysis for individuals

new to CSII therapy. Individuals attending the LCYPDS were invited to attend appointments every 3 months. As HbA1c measures average blood glucose over two to three months, examining HbA1c values by 3 month periods after the CSII start date would be sufficient in detecting any changes in HbA1c values due to CSII therapy. Hospitalisation rates were examined using the same CSII duration groups for comparison.

5.1.4 Cause-specific hospitalisation categorisation.

Hospitalisations were categorised by T1D-related and non-T1D related causes. T1D-related causes for hospitalisation included DKA, severe hypoglycaemia and re-stabilisation/control of diabetes. There was no subgrouping of non-T1D related causes as these were not recorded in the dataset. All other causes for hospitalisation were either categorised as ‘other’ or ‘unknown’ if the cause was not recorded.

5.2 Statistical methodology.

5.2.1 Multi-level modelling to examine differences in HbA1c values before and after continuous subcutaneous insulin infusion (CSII) therapy initiation.

Comparing differences in HbA1c values before and after the start of CSII therapy by using t-tests or ANOVAs would rely on the assumption of independence between observations. In the LCYPDS dataset, repeated HbA1c observations were recorded for the same individuals at different appointment attendances. This violated the assumption of independence and could potentially result in erroneous conclusions with these methodologies. Therefore, multi-level modelling methodology was used to account for these repeated measures within the same individuals by considering the variation between individuals (level 1) as well as within individuals (level 2), reducing bias due to mathematical coupling and regression to the mean compared with single level modelling (137). This modelling approach has previously been used on the LCYPDS cohort (138). In this study, additional analysis included comparisons by CSII duration period, sex and by CSII therapy status.

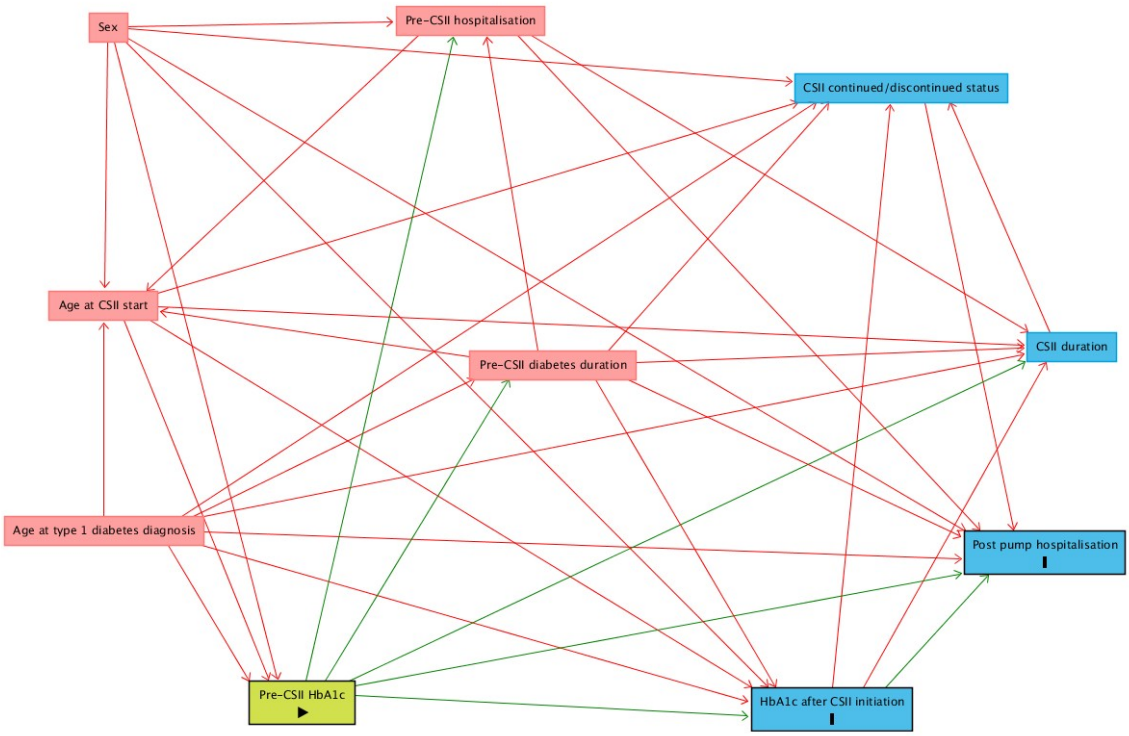
A multi-level random intercept model assumed that the relationship between pre- and during CSII HbA1c values was the same for all individuals. An overall random intercept model was run for the cohort. Separate models were also run by sex and for different CSII duration periods by sex and CSII therapy status.

Multi-level random slope models assumed that the relationship between pre- and during CSII HbA1c values differed between individuals. A random slope model was run to determine if there were any differences between individuals who continued and discontinued CSII. This model was compared by model fit with the equivalent random intercept model by calculating Akaike's information criterion and Bayesian information criterion (Appendix C).

To test whether the multi-level models were better than an ordinary logistic regression model, log likelihood tests were performed.

There was one individual who restarted CSII therapy around 4 years after originally discontinuing CSII therapy. This individual was included twice in the models with a two different level 2 identifiers. Although it could be argued that a previous instance of CSII therapy may influence the results of the second pre-CSII period, it was clinically judged that the gap was long enough for any effect to be at a minimum. As a second CSII therapy occurrence was only found in one individual, it was felt that including their second CSII occurrence with a separate identifier would not have much bias on the overall results.

To determine which variables should be adjusted for in the models, a DAG was completed (Figure 5.1) based on discussions with and advice from clinical specialists. This DAG included pre-CSII HbA1c as the exposure variable and HbA1c and hospitalisation rates after CSII initiation as two outcome variables. The variables sex and age at diabetes diagnosis were found as confounders and were adjusted for in all models. Pre-CSII hospitalisation was found to be a mediator, so was excluded from the models.



Confounders = sex, age at diagnosis

Proxy confounders = age at CSII start, pre-CSII diabetes duration

Mediator = pre-CSII hospitalisation

Figure 5.1: Directed Acyclic Graph (DAG) for multi-level modelling for HbA1c level in the Leeds Children and Young People's Diabetes Service (LCYPDS) cohort.

5.2.2 Calculation of hospitalisation rates.

Hospitalisation rates were calculated for the pre- and during CSII periods by sex, both overall and by CSII status. Hospitalisation rates were calculated by dividing the total number of hospitalisations by the total person-years of follow-up for the whole LCYPDS cohort. Hospitalisation rates were calculated for overall hospitalisations, T1D-related non-T1D related causes.

5.3 Results of analysis from the Leeds Children and Young People's Diabetes Service (LCYPDS).

5.3.1 Demographics.

A total of 161 individuals were included in this study, with one individual with two instances of CSII therapy. Table 5.1 shows the cohort by sex and CSII status with median age of T1D diagnosis and CSII initiation.

Table 5.1: Number (and percentage) of individuals, HbA1c and hospitalisation observations and median (and range) of ages and time periods by sex and continuous subcutaneous insulin infusion (CSII) status.

	Sex		**CSII status**		**Total**
	Males	**Females**	**Continued**	**Discontinued**	
Total individuals	70 (43.2%)	92 (56.8%)	132 (81.5%)	30 (18.5%)	162
Males	-	-	62 (88.6%)	8 (11.4%)	70
Females	-	-	70 (76.1%)	22 (23.9%)	92
Total HbA1c observations – pre-CSII	257 (42.8%)	343 (57.2%)	479 (79.8%)	121 (20.2%)	600
Total HbA1c observations – during CSII	688 (42.5%)	929 (57.5%)	1317 (81.4%)	300 (18.6%)	1,617
Total HbA1c observations – after CSII	62 (44.6%)	77 (55.4%)	-	139 (100%)	139
Total hospitalisations - pre-CSII	19 (33.3%)	38 (66.7%)	42 (73.7%)	15 (26.3%)	57
Total hospitalisations - during CSII	23 (29.1%)	56 (70.9%)	67 (84.8%)	12 (15.2%)	79
Median (range) age at T1D diagnosis	7 (0.9 to 13.7)	5.6 (1.1 to 14.4)	6.3 (0.9 to 13.7)	6.5 (1.1 to 14.4)	6.3 (0.9 to 14.4)
Median (range) age at CSII start	12.1 (1.1 to 17.6)	11.2 (1.9 to 16.7)	11.7 (1.1 to 17.6)	12.7 (6.5 to 16.7)	11.9 (1.1 to 17.6)
Median (range) follow- up pre-CSII	0.8 (0.01 to 1.88)	0.8 (0.04 to 1.97)	0.8 (0.01 to 1.97)	0.8 (0.21 to 1.58)	0.8 (0.01 to 1.97)
Median (range) CSII duration	2.2 (0.1 to 7.1)	2.5 (0 to 8.1)	2.3 (0 to 8.1)	2.5 (0.1 to 5.2)	2.3 (0 to 8.1)

There were more females than males (56.8% vs. 43.2%) in the LCYPDS cohort who started CSII therapy. The percentage of HbA1c observations pre- and during CSII therapy by sex were split similarly to the overall percentages for the total number of individuals by sex. However, the percentage of females with a hospitalisation was greater at around 70% versus 30% in males in both pre- and during CSII time periods (Table 5.1).

There were 30 individuals (18.5%) who discontinued CSII therapy, most of whom were female (n=22; 73.3%). The percentage of pre-CSII hospitalisations by CSII status was higher in the discontinued group (26.3%) compared with the overall percentages for the total number of individuals by CSII status (Table 5.1).

The median ages at T1D onset and CSII start were similar by sex and CSII status. However, where the youngest age at CSII start was 1 year in the continued group, the youngest age at CSII start was 6 years in the discontinued group (Table 5.1).

There were more HbA1c and hospitalisations observations during CSII compared with pre-CSII therapy. Median follow-up time from first recorded pre-CSII HbA1c value to CSII initiation was around three times shorter that the median CSII therapy duration (0.8 years (range 0.01 to 1.97 years) vs. 2.3 years (range 0 to 8.1 years)) (Table 5.1). Therefore, there was less follow-up time pre-CSII for HbA1c observations and hospitalisations to occur compared with the CSII.

There were more T1D-related hospitalisations compared with non-T1D related hospitalisations, both pre- and during CSII. The overall percentage of T1D-related hospitalisations was around 10% higher in the discontinued CSII group (n=11; 73.3%) compared with those who continued CSII (n=25; 59.5%) for the pre-CSII period (Table 5.2). There were no hospitalisations recorded for the discontinued CSII group after a CSII end date.

5.3.2 HbA1c levels before and after the initiation of continuous subcutaneous insulin infusion (CSII).

For the overall cohort, the median HbA1c value pre-CSII was 8.9% (range 5.5 to 15.9%) compared with 8.3% (range 5.4 to 14.4%) during CSII (Table 5.3).

Table 5.2: Number (and percentage) of hospitalisations by sex and continuous subcutaneous insulin infusion (CSII) status.

		Hospitalisation type				
CSII period and CSII status	**Sex**	**T1D-related**	**DKA**	**Severe hypoglycaemia**	**Non-T1D related**	**Total***
Pre-CSII: all	All	36 (63.2%)	15 (26.3%)	8 (14%)	10 (17.5%)	57
	Males	12 (63.2%)	2 (10.5%)	4 (21.1%)	4 (21.1%)	19
	Females	24 (63.2%)	13 (34.2%)	4 (10.5%)	6 (15.8%)	38
Pre-CSII: continued CSII	All	25 (59.5%)	14 (33.3%)	3 (7.1%)	7 (16.7%)	42
	Males	7 (50%)	2 (14.3%)	0	4 (28.6%)	14
	Females	18 (64.3%)	12 (42.9%)	3 (10.7%)	3 (10.7%)	28
Pre-CSII: discontinued CSII	All	11 (73.3%)	14 (93.3%)	5 (33.3%)	3 (20%)	15
	Males	5 (100%)	0	4 (80%)	0	5
	Females	6 (60%)	1 (10%)	1 (10%)	3 (30%)	10
During CSII: all	All	43 (54.4%)	27 (34.2%)	6 (7.6%)	22 (27.8%)	79
	Males	14 (60.9%)	11 (47.8%)	1 (4.3%)	7 (30.4%)	23
	Females	29 (51.8%)	16 (28.6%)	5 (8.9%)	15 (26.8%)	56
During CSII: continued CSII	All	35 (52.2%)	20 (29.9%)	6 (9%)	21 (31.3%)	67
	Males	13 (65%)	10 (50%)	1 (5%)	6 (30%)	20
	Females	22 (46.8%)	10 (21.3%)	5 (10.6%)	15 (31.9%)	47
During CSII: discontinued CSII	All	8 (66.7%)	7 (58.3%)	0	1 (8.3%)	12
	Males	1 (33.3%)	1 (33.3%)	0	1 (33.3%)	3
	Females	7 (77.8%)	6 (66.7%)	0	0	9

*Total includes ‘Unknown’ hospitalisation type.

Table 5.3: HbA1c values by sex, continuous subcutaneous insulin infusion (CSII) period and CSII status.

CSII period and CSII status	Sex	Total HbA1c observations	Mean HbA1c value (%)	Median (range) HbA1c value (%)	Standard deviation of HbA1c value (%)
Pre-CSII: all	All	600	9.2	8.9 (5.5 to 15.9)	1.6
	Males	257	9.2	9.1 (5.5 to 14.7)	1.5
	Females	343	9.1	8.8 (6.2 to 15.9)	1.7
Pre-CSII: continued CSII	All	479	9.0	8.8 (5.5 to 15.9)	1.5
	Males	225	9.2	9.1 (5.5 to 14.7)	1.6
	Females	254	8.8	8.7 (6 to 15.9)	1.5
Pre-CSII: discontinued CSII	All	121	9.9	9.5 (7.1 to 14)	1.7
	Males	32	9.6	9.45 (7.4 to 12.8)	1.3
	Females	89	10.0	9.5 (7.1 to 14)	1.8
During CSII: all	All	1,617	8.5	8.3 (5.4 to 14.4)	1.4
	Males	688	8.4	8.2 (5.4 to 14.04)	1.4
	Females	929	8.6	8.4 (5.5 to 14.4)	1.4
During CSII: continued CSII	All	1,317	8.3	8.2 (5.4 to 12.8)	1.2
	Males	614	8.3	8.1 (5.4 to 12.8)	1.2
	Females	703	8.3	8.28 (5.5 to 12.6)	1.2
During CSII: discontinued CSII	All	300	9.5	9.2 (5.6 to 14.4)	1.8
	Males	74	9.5	9.3 (6.5 to 14.04)	1.8
	Females	226	9.5	9.2 (5.6 to 14.4)	1.8
After CSII: discontinued CSII	All	139	9.5	9.1 (6.2 to 14.04)	1.9
	Males	62	9.1	8.85 (6.2 to 12.1)	1.3
	Females	77	9.8	9.3 (6.9 to 14.04)	2.2

The results from the random intercept model for the overall cohort found a significantly higher reduction in mean HbA1c value during CSII of 0.62% (95% CI 0.53% to 0.72%) (Table 5.4).

Table 5.4: Mean HbA1c value change during (and after) continuous subcutaneous insulin infusion (CSII) therapy from pre-CSII values by CSII period and status and sex.

CSII period and CSII status	Sex	Mean HbA1c value change (and 95% CI) from pre-CSII vales (%)
During CSII – all	All	**-0.62 (-0.72 to -0.53)***
	Males	**-0.78 (-0.92 to -0.64)***
	Females	**-0.5 (-0.63 to -0.38)***
During CSII – continued CSII	All	**-0.67 (-0.77 to -0.58)***
	Males	**-0.86 (-1 to -0.72)***
	Females	**-0.51 (-0.64 to -0.38)***
During CSII – discontinued CSII	All	**-0.43 (-0.71 to -0.15)***
	Males	-0.12 (-0.64 to 0.4)
	Females	**-0.54 (-0.87 to -0.21)***
After CSII discontinuation - discontinued CSII	All	0.11 (-0.23 to 0.44)
	Males	-0.03 (-0.57 to 0.51)
	Females	0.25 (-0.17 to 0.67)

*Statistically significant decrease in mean HbA1c value from pre-CSII values

Random intercept models by CSII duration found that there was an overall significant decrease in HbA1c maintained for up to 4 years (Figure 5.2).

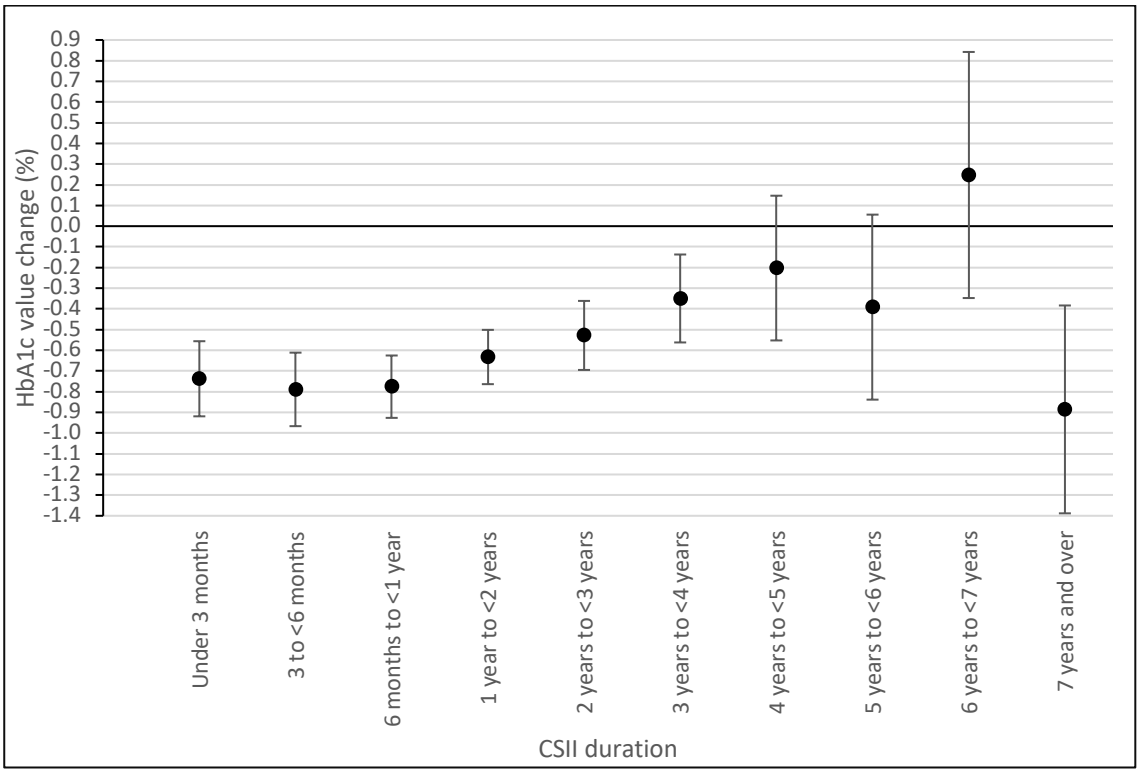


Figure 5.2: Mean HbA1c value change during continuous subcutaneous insulin infusion (CSII) therapy from pre-CSII values by CSII duration.

After 4 years, HbA1c values returned to pre-CSII levels until 7 years CSII duration. The 7 years and over category had the largest change in HbA1c with a decrease of 0.89% (0.38 to 1.39%), although small numbers were observed in this category (Table 5.5).

Table 5.5: Number of individuals and mean HbA1c value change during continuous subcutaneous insulin infusion (CSII) therapy from pre-CSII values by CSII duration.

CSII duration	Total individuals	Mean HbA1c value change (and 95%CI) from pre-CSII value (%)
Under 3 months	132	**-0.74 (-0.92 to -0.56)***
3 to <6 months	133	**-0.79 (-0.97 to -0.61)***
6 months to <1 year	142	**-0.78 (-0.93 to -0.63)***
1 year to <2 years	130	**-0.63 (-0.76 to -0.5)***
2 years to <3 years	93	**-0.53 (-0.7 to -0.36)***
3 years to <4 years	63	**-0.35 (-0.56 to -0.14)***
4 years to <5 years	36	-0.2 (-0.55 to 0.15)
5 years to <6 years	20	-0.39 (-0.84 to 0.06)
6 years to <7 years	15	0.25 (-0.35 to 0.84)
7 years and over	4	**-0.89 (-1.39 to -0.38)***

*Statistically significant decrease in mean HbA1c value from pre-CSII values
**Statistically significant increase in mean HbA1c value from pre-CSII values

5.3.3 Hospitalisation rates before and after the initiation of continuous subcutaneous insulin infusion (CSII).

The overall incidence rate of all hospitalisations was significantly higher during CSII (24.27 per 100 person-years (95%CI 19.47 to 30.26 per 100 person-years)) compared to pre-CSII (8.39 per 100 person-years (95%CI 6.48 to 10.88 per 100 person-years) (Table 5.6).

Table 5.6: Hospitalisation incidence rates per 100 person-years (and 95%CI) by sex, hospitalisation type, CSII period and CSII status in the LCYPDS.

CSII period and CSII status	Sex	All hospitalisations	T1D-related	DKA	Severe hypoglycaemia	Non-T1D related
Pre-CSII: all	All	8.39 (6.48 to 10.88)	5.22 (3.77 to 7.24)	2.16 (1.3 to 3.59)	1.13 (0.57 to 2.27)	1.45 (0.78 to 2.7)
	Males	6.8 (4.34 to 10.66)	4.17 (2.37 to 7.34)	0.69 (0.17 to 2.76)	1.36 (0.51 to 3.63)	1.41 (0.53 to 3.76)
	Females	9.51 (6.92 to 13.07)	5.98 (4.01 to 8.93)	3.22 (1.87 to 5.55)	0.97 (0.36 to 2.59)	1.49 (0.67 to 3.31)
Pre-CSII: continued CSII	All	7.73 (5.71 to 10.46)	4.52 (3.05 to 6.69)	2.52 (1.49 to 4.25)	0.53 (0.17 to 1.64)	1.27 (0.61 to 2.67)
	Males	5.56 (3.29 to 9.39)	2.69 (1.28 to 5.64)	0.77 (0.19 to 3.06)	-	1.57 (0.59 to 4.17)
	Females	9.59 (6.62 to 13.89)	6.14 (3.87 to 9.74)	4.07 (2.31 to 7.16)	0.99 (0.32 to 3.08)	1.02 (0.33 to 3.15)
Pre-CSII: discontinued CSII	All	11.08 (6.68 to 18.37)	8.11 (4.49 to 14.65)	2.52 (1.49 to 4.25)	3.64 (1.52 to 8.76)	2.19 (0.71 to 6.78)
	Males	17.94 (7.47 to 43.1)	17.94 (7.47 to 43.1)	-	14.25 (5.35 to 7.98)	-
	Females	9.3 (5 to 17.28)	5.57 (2.5 to 12.39)	0.92 (0.13 to 6.53)	0.92 (0.13 to 6.51)	2.75 (0.89 to 8.53)
During CSII: all	All	**24.27 (19.47 to 30.26)***	**12.06 (8.94 to 16.26)***	**7.4 (5.08 to 10.8)***	1.48 (0.67 to 3.3)	**5.85 (3.85 to 8.88)***
	Males	**16.12 (10.71 to 24.26)***	9.23 (5.47 to 15.58)	**7.15 (3.96 to 12.91)***	0.59 (0.08 to 4.21)	4.36 (2.08 to 9.15)
	Females	**30.63 (23.57 to 39.8)***	**14.15 (9.83 to 20.36)***	7.59 (4.65 to 12.39)	2.11 (0.88 to 5.08)	**6.95 (4.19 to 11.54)***

During CSII: continued CSII	All	**25.05 (19.72 to 31.83)***	**11.84 (8.5 to 16.5)***	6.56 (4.23 to 10.16)	1.8 (0.81 to 4)	**6.86 (4.47 to 10.52)***
	Males	15.84 (10.22 to 24.55)	9.68 (5.62 to 16.66)	**7.32 (3.94 to 13.61)***	0.67 (0.09 to 4.73)	4.19 (1.88 to 9.33)
	Females	**33.29 (25.01 to 44.31)***	13.65 (8.99 to 20.73)	5.93 (3.19 to 11.03)	2.72 (1.13 to 6.54)	-
During CSII: discontinued CSII	All	20.69 (95%CI 11.75 to 36.44)	13.08 (95%CI 6.54 to 26.16)	**11.74 (95%CI 5.6 to 24.62)**	-	1.43 (95%CI 0.2 to 10.13)
	Males	18.35 (95%CI 5.92 to 56.89)	5.77 (95%CI 0.81 to 40.97)	5.77 (95%CI 0.81 to 40.97)	-	5.76 (95%CI 0.81 to 40.91)
	Females	21.61 (95%CI 11.25 to 41.54)	15.97 (95%CI 7.61 to 33.5)	14.18 (95%CI 6.37 to 31.57)	-	-

*Statistically significant increase in hospitalisation incidence rate during CSII from pre-CSII rates.

There were also significant increases in hospitalisation incidence during CSII compared with pre-CSII incidence for T1D-related hospitalisation, DKA and non-T1D-related hospitalisations. The increase in DKA incidence was over 3-fold (Table 5.6). There was no significant difference between pre- and during CSII incidence for severe hypoglycaemia.

Analysis by CSII duration found that DKA hospitalisations were significantly higher compared with pre-CSII levels for up to one year of therapy (Figure 5.3).

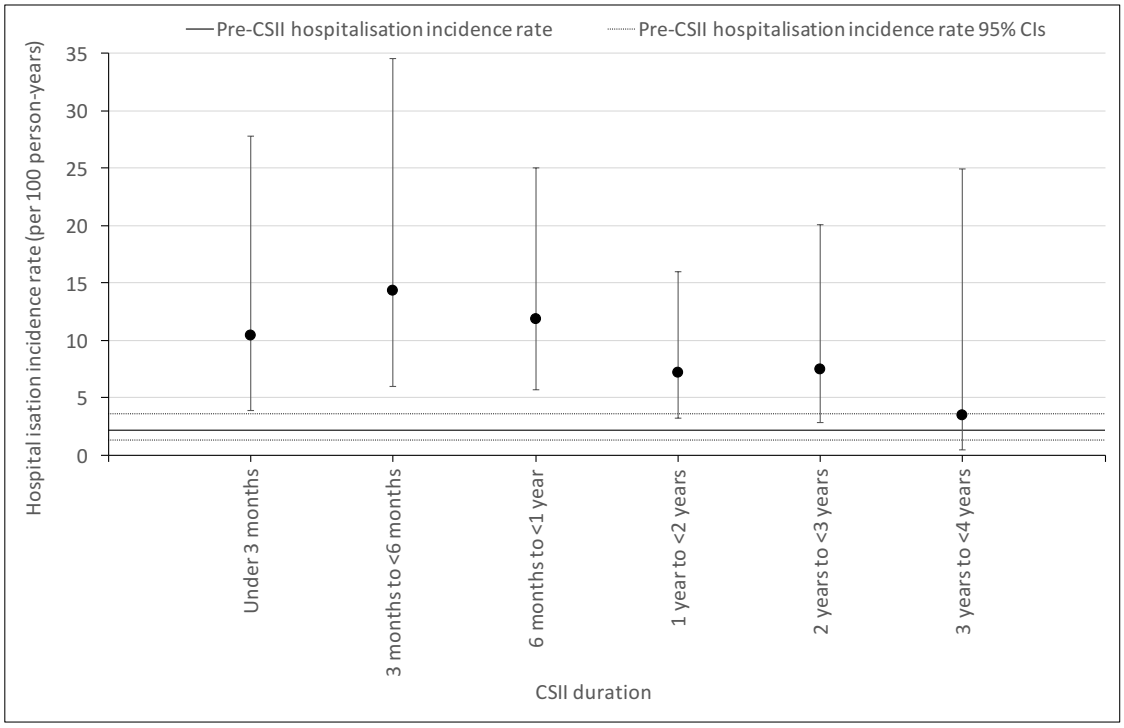


Figure 5.3: Hospitalisation incidence rate per 100 person-years of diabetic ketoacidosis (DKA) by continuous subcutaneous insulin infusion (CSII) duration.

For severe hypoglycaemia, there were no significant differences in hospitalisation incidence rate during any time period of CSII duration compared with pre-CSII incidence (Figure 5.4).

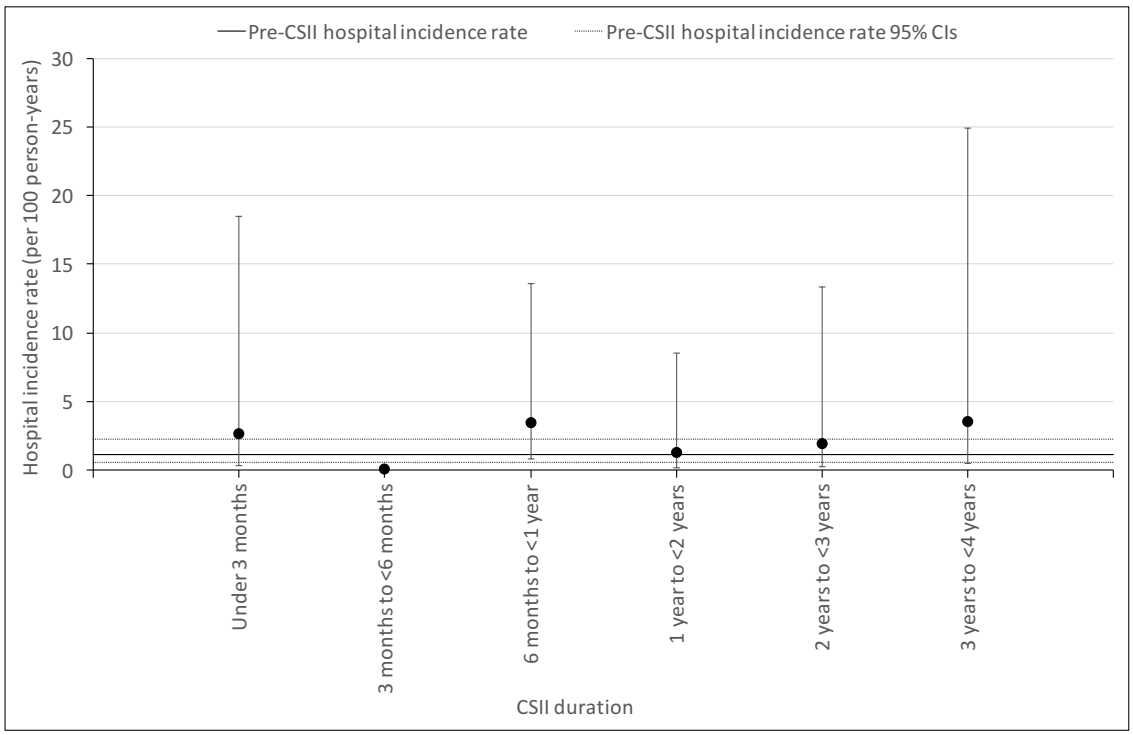


Figure 5.4: Hospitalisation incidence rate per 100 person-years of severe hypoglycaemia by continuous subcutaneous insulin infusion (CSII) duration.

5.3.4 HbA1c change and hospitalisation rates by sex.

Table 5.3 showed that there were similar HbA1c means and medians between males and females for the cohort overall during the pre-CSII cohort. There was a lower HbA1c mean and median for females in the continued group pre-CSII but a slightly higher HbA1c level was found in the discontinued group. However, these differences between the sexes were not found to be significant.

Table 5.4 showed significant decreases in HbA1c overall and in the continued group for both sexes during CSII. For the discontinued groups, only females saw a significantly decrease during CSII therapy and no change in HbA1c was found in males. After CSII discontinuation, HbA1c levels were no different from pre-CSII level for both sexes, even in females where an improvement was found during CSII.

Figure 5.5 showed that a significant decrease from pre-CSII values for HbA1c was sustained up to 6 years CSII duration for all males.

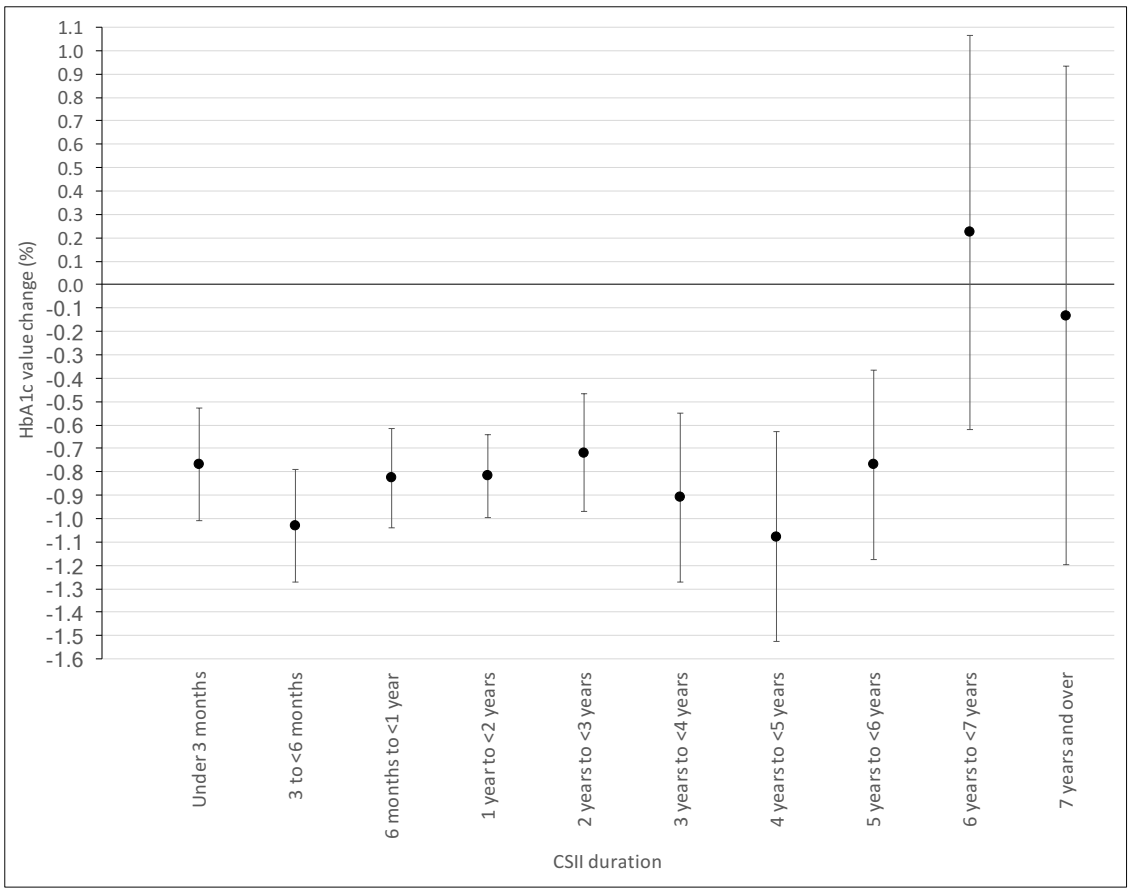


Figure 5.5: Mean HbA1c value change during (and after) continuous subcutaneous insulin infusion (CSII) therapy from pre-CSII values by CSII duration for males.

However, this improvement was only sustained for up to 3 years CSII duration in females (Figure 5.6).

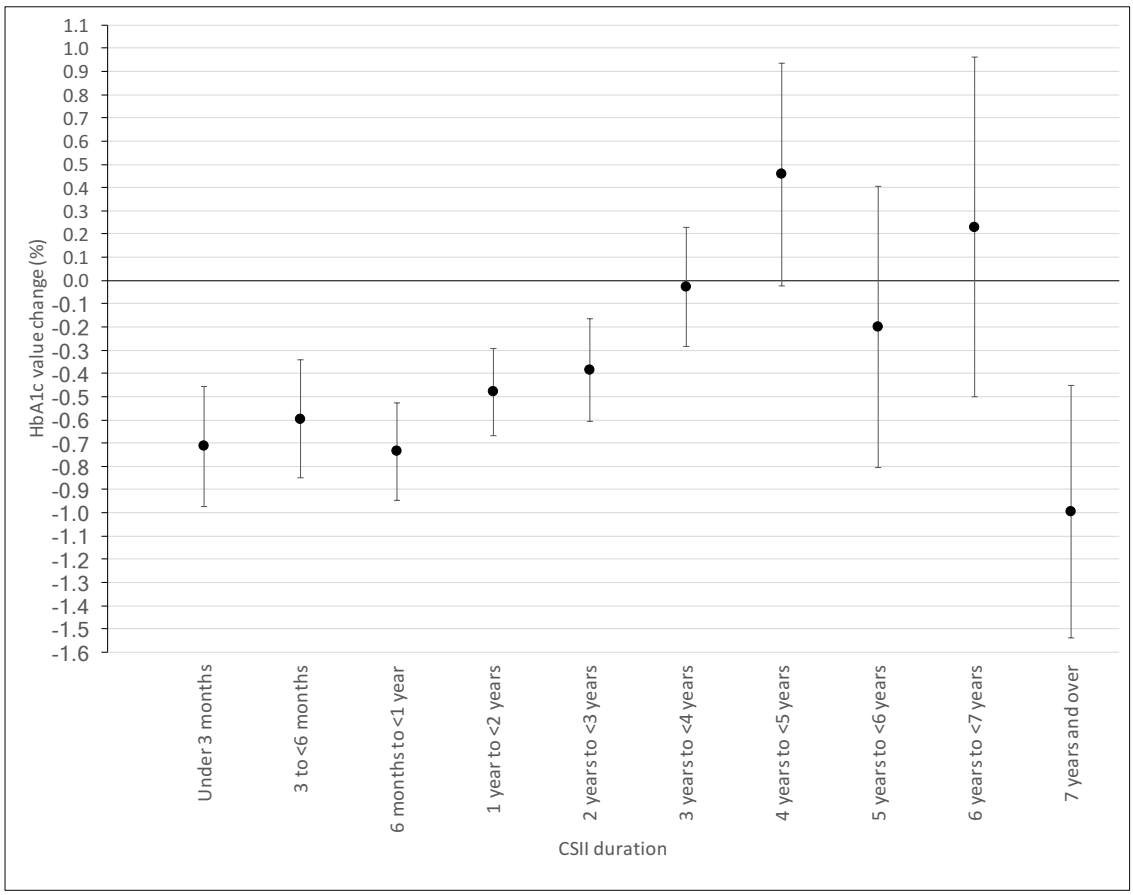


Figure 5.6: Mean HbA1c value change during (and after) continuous subcutaneous insulin infusion (CSII) therapy from pre-CSII values by CSII duration for females.

For hospitalisations, there was a significant increase in overall hospitalisations in males and females during CSII compared to pre-CSII. Although there was a significant increase in all T1D-related hospitalisations during CSII in females, there were no significant differences from pre-CSII rates for DKA and severe hypoglycaemia during CSII therapy. However, there were increases in DKA hospitalisations during CSII compared with pre-CSII rates for males for both the continued group (Table 5.6).

5.3.5 HbA1c change and hospitalisation rates by continuous subcutaneous insulin infusion (CSII) status.

The continued CSII group had a similar median HbA1c value pre-CSII compared with the overall cohort. The discontinued group had a higher median pre-CSII value at 9.5% (range 7.1 to 14%), although this was not statistically significantly higher than the continued group (Table 5.3).

The random intercept models found significant decreases in HbA1c values during CSII therapy from pre-CSII values for both the continued and discontinued groups. The decrease was less for the discontinued group at 0.43% (95%CI 0.15 to 0.71%) compared with the continued group (0.67% (95%CI 0.58 to 0.77%) (Table 5.4). There was no significant difference in HbA1c decrease between the continued and discontinued groups.

By duration, those who continued CSII therapy had a significant decrease in HbA1c value from pre-CSII values during CSII for up to 5 years (Figure 5.7). For those who discontinued CSII, improvements in HbA1c was only sustained up to the first year of CSII duration (Figure 5.8).

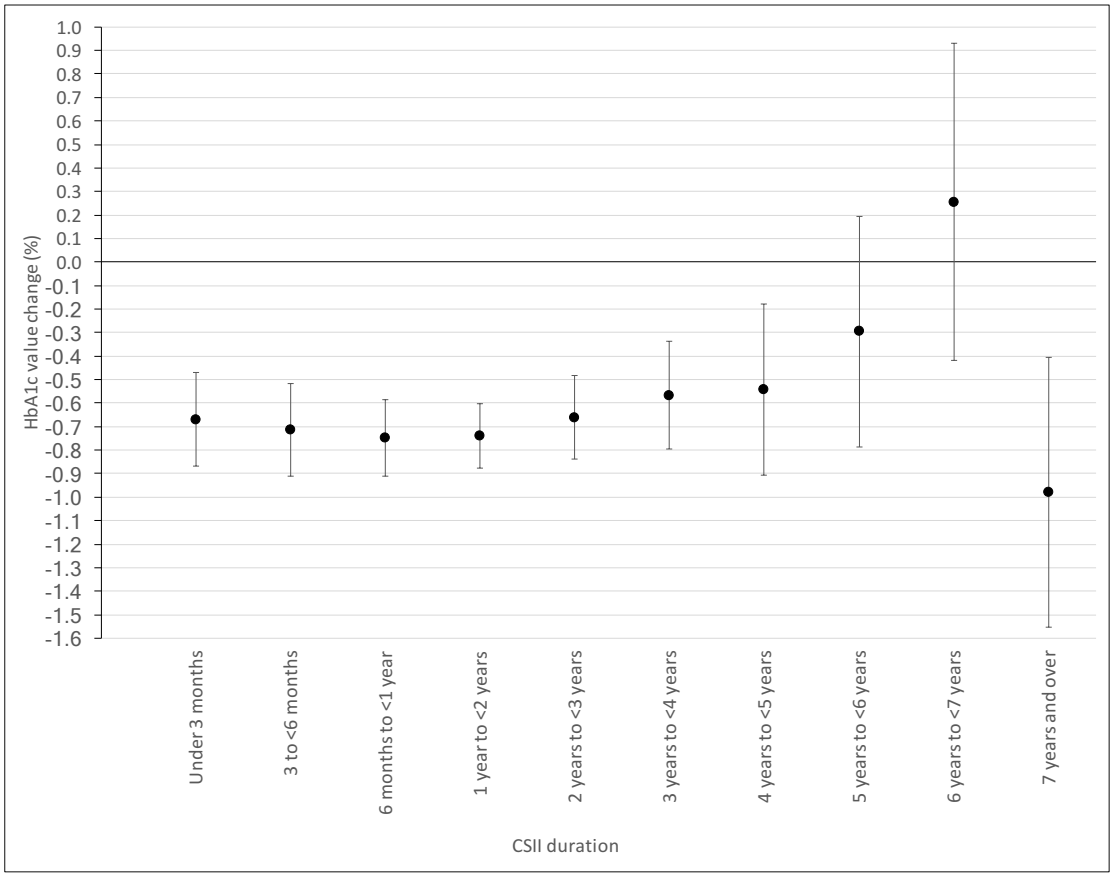


Figure 5.7: Mean HbA1c value change during (and after) continuous subcutaneous insulin infusion (CSII) therapy from pre-CSII values by CSII duration for individuals who continued CSII therapy.

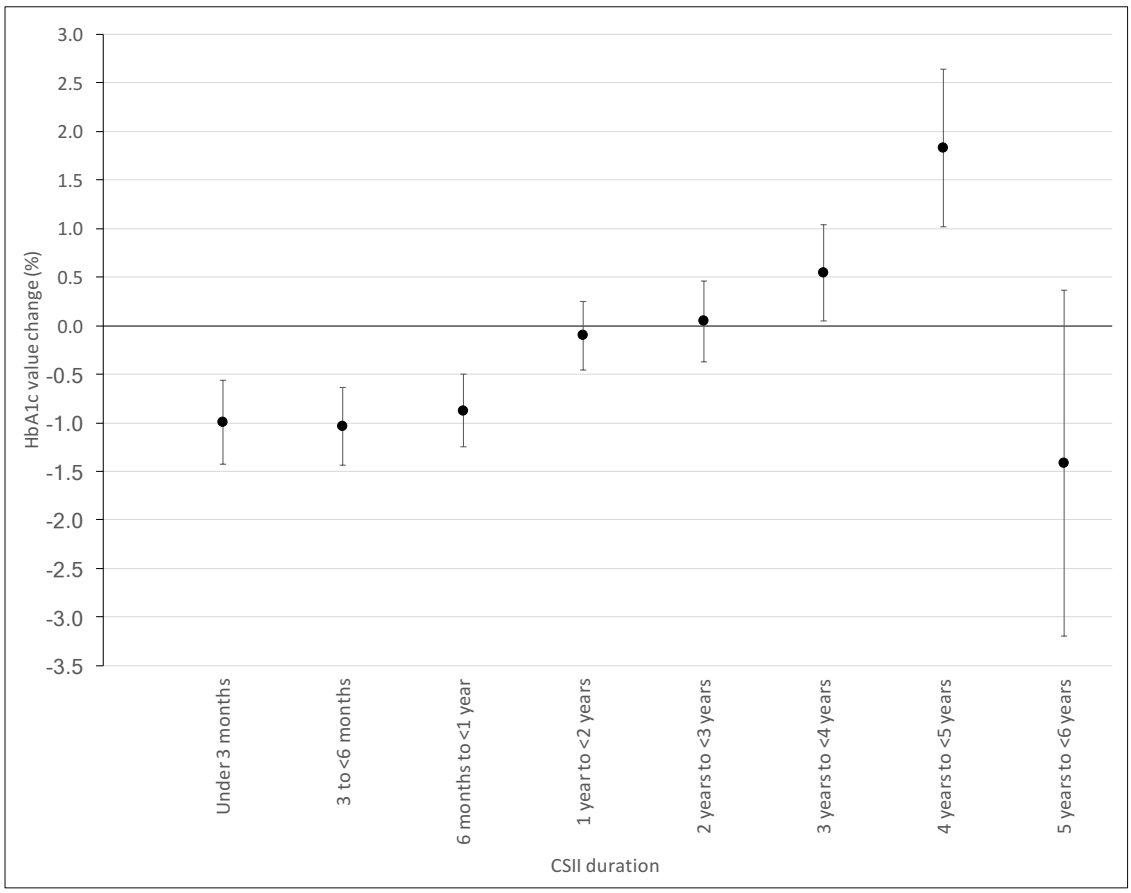


Figure 5.8: Mean HbA1c value change during (and after) continuous subcutaneous insulin infusion (CSII) therapy from pre-CSII values by CSII duration for individuals who discontinued CSII therapy.

There was a significant increase in overall hospitalisations for the continued group during CSII compared with pre-CSII hospitalisations. For the discontinued group, there was no significant difference for overall hospitalisations during CSII compared with pre-CSII. Only DKA for the discontinued group saw a significant increase during CSII therapy (Table 5.6).

5.4 Summary of results.

There was a significant reduction in HbA1c values during CSII therapy compared with pre-CSII values. Overall, this reduction was sustained up to 4 years of CSII duration, before HbA1c returned to pre-CSII levels. However, males were shown to have an extended period of sustained improvement of up to 6 years, whereas females had a shorter duration of improvement of up to 3 years.

Females were also more likely to discontinue CSII therapy. However, the discontinued males showed no improvement in HbA1c values during CSII, in

contrast to females who did have significantly lower HbA1c values during CSII compared with pre-CSII values. For both males and females who discontinued CSII, there were no significant differences in HbA1c values between pre-CSII and after CSII periods.

Despite improvements in HbA1c, hospitalisation rates increased with CSII therapy in the continued CSII group. No significant increase in hospitalisations, apart from DKA were found in the discontinued group. Analysis by CSII duration found that DKA increased during CSII, particularly in the first year of CSII therapy. There were no significant differences in severe hypoglycaemia between pre- and during CSII time periods.

5.5 Overall summary analysis compared with previous studies.

With a maximum of 8 years follow-up time, the LCYPDS showed improved HbA1c levels during CSII therapy for up to 4 years. The few previous studies with more than 5 years follow-up time showed that improved HbA1c levels were maintained for between 2 to 6 years of CSII therapy (276,277), so the results from the LCYPDS fall mid-way between this period.

In previous research, the highest reported proportion of discontinuation of CSII therapy was 11.3% (150). The LCYPDS found a higher proportion of 18.3%. Those who eventually discontinued CSII therapy had similar overall HbA1c improvements with CSII therapy compared with those who continued. However, after discontinuation of CSII HbA1c increased to pre-CSII levels. This provided evidence for the clinical importance of remaining on CSII therapy to lower HbA1c levels.

For hospitalisations, severe hypoglycaemia incidence did not change with CSII therapy. In other studies, only a few found no change in hospitalisation for hypoglycaemia after CSII (136,146). Many other studies have shown a decrease in hospitalisations during CSII (130,132,278–281,135,139–145). An explanation for these differences may be due to the inconsistency between studies in defining severe hypoglycaemia and distinguishing between mild and severe episodes. In this study, severe hypoglycaemia was defined as an inpatient admission or an A&E attendance. Treatment without hospitalisation, for example, treatment from ambulance services, were not included. This may give an underestimation of total cases of severe hypoglycaemia in the cohort.

Research on DKA hospitalisations showed more variation, with some studies showing lower rates of DKA hospitalisation with CSII therapy (134,140,141,145), whilst other studies have found no change in DKA

hospitalisation incidence (136,143,146,147). Few studies have reported higher DKA hospitalisation rates (131,144), consistent with findings from the LCYPDS. Recent national findings from the latest NPDA report have also suggested that CSII therapy increased the risk of a DKA admission (126). Contrary to results from the LCYPDS where an increase in DKA admissions was limited to the first year of CSII therapy, the NPDA found that an increased risk of a DKA admission was associated with longer duration of diabetes. It is difficult to compare the results of this study with national data from the logistic regression model used in the NPDA, as this included individuals up to 25 years and individuals on MDIs. However, both results showed the need to address this increase in DKA admissions rates at both a national and local level.

5.6 Health outcomes by attained age groups.

Hospitalisation for DKA was found to be high in the LCYPDS cohort, particularly in the first year of CSII treatment. DKA often occurs due to poor management of T1D. This increase in DKA deaths and hospitalisations during the transitional care period may indicate problems with self-management. Recurrent DKA hospital admissions have also been shown to be higher at younger ages (282) and could increase the risk of mortality (270).

5.7 Health outcomes by socio-demographic groups.

Overall, females had less sustained improvement in HbA1c levels with CSII therapy compared with males in the LCYPDS. The decrease in HbA1c levels was sustained for longer in males by 3 years and over twice the proportion of females discontinued CSII compared with males (23.9% vs. 11.4%). Of those who discontinued CSII, HbA1c values for males showed no significant differences to pre-CSII levels during CSII, whilst females had improved HbA1c levels. These gender differences have previously been reported in survey data in a recent study by Tanenbaum and colleagues. They found that even though females had higher CSII therapy uptake, females identified more barriers with using the CSII device, contributing to higher levels of distress and more concerns about body image due to the attachment of the CSII device (39). Ritholz and colleagues also reported body image concerns from female adults and these attitudes were associated with HbA1c values (40). This suggested clear gender differences with CSII therapy which need to be addressed with specialist intervention.

Outcomes by ethnicity and deprivation could not be examined in the LCYPDS cohort due to the unavailability of these data items. No previous studies have assessed HbA1c and hospitalisations with CSII therapy by ethnicity and deprivation, so it is not known whether these are predictors for negative health outcomes.

5.8 Chapter summary.

Hospitalisation for DKA was found to be high in the LCYPDS cohort, particularly in the first year of CSII treatment. Whether this is associated with an increased rate of DKA death in the YRDCYP cannot be verified. Overall, females had half the length of sustained improvement in HbA1c levels with CSII therapy compared with males in the LCYPDS and were more likely to discontinue. More females were also starting CSII therapy. This suggests that females are having more issues with HbA1c and CSII therapy. This is in contrast to the mortality data for the YRDCYP which found more deaths in males. Without data from the LCYPDS, these differences between sexes during different aspects of the treatment journey would could be identified.

Chapter 6 Cancer hospitalisations.

This chapter describes the methodology and results of analysis from data on the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) cohort. The YSRCCYP was linked to Hospital Episode Statistics (HES) data (inpatient, outpatient and A&E datasets) and the Mental Health Minimum Dataset (MHMDS). Each HES dataset and the MHMDS were examined separately and were also combined to measure the following health outcomes:

1. Mental health admission by age at first known admission and cancer type.
2. Outpatient appointment by attendance status, age at appointment, cancer type and complication type.
    a. Outpatient appointment attendance status following a first known mental health admission.
3. Inpatient admissions by age at inpatient admission, cancer type and complication type.
    a. Inpatient admission following a first known mental health admission.
    b. Inpatient admission within 90 days of an outpatient appointment by attendance status.
4. A&E attendances by age at A&E attendance and cancer type.
    a. A&E attendance following a first known mental health admission.
    b. A&E within 90 days of an outpatient appointment by attendance status.

Analysis of health outcomes using the HES datasets covered the follow-up period of 5 years since initial cancer diagnosis. The MHMDS and inpatient data were used to determine first known mental health admissions recorded before, on or after the date of initial cancer diagnosis. It was possible for individuals to have multiple occurrences of outpatient appointments, A&E attendances and inpatient admissions. Mental health admission analysis categorised individuals as either having received or not received a mental health admission at any time.

This chapter begins by defining variable categorisations and continues with defining the statistical approach used in the analysis and reports the results from these data analyses. All analyses were performed using STATA 14 (257).

6.1 Variable definitions.

The methodologies for defining cancer type diagnosis and the follow-up period were described in section 3.3.1.

6.1.1 Age categories at cancer diagnosis.

Individuals from the YSRCCYP diagnosed with cancer before the transitional care period (under 15 years) were described as having ‘early cancer onset’. Individuals diagnosed during the transitional care period (15 to 29 years) were described as having ‘late cancer onset’.

6.1.2 Defining complication type.

The HES inpatient and outpatient datasets included up to 12 diagnosis code fields, using ICD-10 coding. These fields described the type of complication an individual was receiving hospital treatment for. In this analysis, only the first diagnosis code was included in the analysis and categorised by ICD-10 chapter groups (see Appendix D).

Unfortunately, diagnosis codes were incomplete for HES outpatient data as there was no mandatory collection for these variables. As a proxy, the treatment specialty field was used instead of diagnosis. Treatment specialty was defined as the “specialised service within which the patient was treated” (260, p.302). There were over 200 codes for treatment specialty, with no standardised groupings as with ICD-10 codes. Therefore, clinical guidance was needed to group treatment specialty for analysis (see Appendix E). To compare inpatient complications with outpatient data, inpatient data were also analysed by treatment specialty. If an individual had more than one outpatient appointment on the same day at different treatment specialities, all outpatient appointments were included in the outpatient analysis.

The inpatient data were analysed at continuous inpatient spell (CIPS) level (defined in section 3.3.5.5). Therefore, inpatient admissions occurring on the same day would count as being part of the same CIPS. The admission with the earliest admission time was used to categorise the complication type for the CIPS.

6.1.3 Outpatient appointment data – did not attend (DNA) status.

The ‘ATTENDED’ variable in the outpatient HES data determined the attended status for an appointment. For this analysis, these codes were categorised as either ‘Attended’, ‘Did not attend’ (DNA) or ‘Unknown’ (Table 6.1).

Table 6.1: Codes for 'ATTENDED' field in outpatient HES data and categorisation for analysis.

Code	Code description	Attended/Did not attend (DNA) status
2	Appointment cancelled by, or on behalf of, the patient	Attended
3	Did not attend – no advance warning given	DNA
4	Appointment cancelled or postponed by the Health Care Provider	Attended
5	Seen, having attended on time or, if late, before the relevant care professional was ready to see the patient	Attended
6	Arrived late, after the relevant care professional was ready to see the patient, but was seen	Attended
7	Did not attend – patient arrived late and could not be seen	DNA
9	Not known	Not known

6.1.4 Accident and emergency (A&E) – arrival mode.

The A&E arrival mode described how a patient arrived at A&E. A&E attendances were either categorised by ‘Ambulance’ (this included helicopter or air ambulance), ‘Other’ or ‘Unknown’.

6.1.5 Earliest recorded mental health admission from Mental Health Minimum Data set (MHMDS) and mental health inpatient data.

The MHMDS included a date field for the first known mental health admission. This included dates before the coverage period for the MHMDS dataset, i.e. before 01/04/2007. Individuals were also included in the mental health data if they had a mental health-related inpatient admission with a primary diagnosis ICD-10 code between F01 to F99 (mental behavioural and neurodevelopmental disorders). If these individuals were not identified from the MHMDS, the date of earliest admission on the inpatient data was used as the recorded first mental health admission. These individuals were also included in the inpatient analysis.

6.2 Statistical methodology.

6.2.1 Incidence rates for outpatient appointment non-attendance, accident and emergency (A&E) attendance, inpatient and mental health admissions.

Incidence rates for the follow-up period were calculated for outpatient appointments with a DNA status, A&E attendances and CIPS by age at onset group. To compare incidence rates with the HES datasets, incidence rates of mental health admissions were also calculated for the follow-up period only. These incidence rates were calculated by dividing the total number of outpatient appointments with a DNA status, A&E attendances, inpatient CIPS and first known mental health occurrence by the total person-years of follow-up from 5 years after cancer diagnosis date. The incidence rates were expressed as per 1,000 person-years with a 95% confidence interval calculated using the Poisson distribution. Incidence rates by age, sex, ethnicity, deprivation and cancer type were calculated for comparison against total cohort rates.

6.2.2 Confounder variables for statistical modelling.

Confounder variables included in all statistical models were determined by DAGs based on discussions with and advice from clinical specialists. DAGs for all statistical models where the exposure variable was either age at hospitalisation or cancer type found the variables sex, deprivation and ethnicity to be confounders (see Appendix F). As age at cancer onset was not found to be a confounder variable in any DAGs, separate models were run for early and late cancer onset groups. Additionally, as age at cancer onset was associated with cancer type, producing separate models prevented issues around collinearity. Reference groups for each variable included in the models are presented in Table 6.2.

Table 6.2: Reference groups for variables included in statistical models.

Variable	Reference group
Age at hospitalisation – early cancer onset	10 to 14 years
Age at hospitalisation – late cancer onset	40 and over years
Sex	Males
Ethnicity	White
Deprivation	Least deprived fifth
Cancer type – early cancer onset	IV Neuroblastoma
Cancer type – late cancer onset	VIII Malignant bone
Treatment specialty (outpatient data)	Oncology
Diagnosis type (inpatient data)	Neoplasms

The reference groups were chosen for their ease of interpretation of results. The choice of reference groups did not alter the results of the model. The cancer type reference groups were different for each age at cancer onset group due to the differences of prevalence of certain cancer types by age. Therefore, different reference cancer types were determined separately for each age at onset group.

6.2.3 Single-level and mixed effects Poisson regression.

Mixed effects Poisson regression was used to determine which variables were predictors for the relative risk of A&E attendance and inpatient admissions. A multi-level modelling approach was used to account for repeated attendances and admissions within the same individual. For mental health analysis, only the first known mental health admission was included in analysis. As there was no repeated data for individuals, a single-level Poisson modelling approach was used. To prevent issues around collinearity due to associations between cancer type with age at cancer onset, treatment specialty and diagnosis type, separate models were performed for age at cancer onset group, cancer type, treatment specialty and diagnosis type.

6.2.4 Mixed effects logistic regression.

To compare the odds of an DNA outpatient appointment compared with an attended appointment and to determine which variables were predictors for the odds of a DNA appointment, mixed effects logistic regression was used. Mixed effects logistic regression accounted for repeated measures within the same individual and reduced bias compared with single-level logistic regression. As with the Poisson regression models, separate models were performed for age at cancer onset group, cancer type and treatment specialty to prevent issues surrounding collinearity. Odds ratios were equivalent to relative risk for rare events, where the outcome was 10% or less (284).

6.2.5 Sensitivity analysis.

Due to the differences in time coverage of the YSRCCYP dataset and HES datasets (Figure 3.7), the HES data were not complete for all individuals so results may have exhibited selection bias. To assess this bias, sensitivity analysis was conducted for outpatient, inpatient and A&E data, whereby the statistical analysis was completed for a subset of the YSRCCYP, excluding any

individuals diagnosed more than 5 years before the start date of the beginning of the HES coverage period.

If an individual had a mental health admission before 01/04/2007 but had no other mental health admissions during the MHMDS coverage period (01/04/2007 to 31/03/2015), these individuals could not be identified in our analysis. This would also cause selection bias in results, as with the other HES datasets which did not cover the entire time period of the YSRCCYP cohort. However, sensitivity analysis was not completed for the mental health data as there would have been difficulty in determining the sensitivity cohort without creating further bias. For example, only including individuals diagnosed with cancer since 01/04/2007 would exclude a large proportion of individuals with a mental health admission after their initial cancer diagnosis.

6.3 Results of analysis from the Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP).

6.3.1 Demographics.

There were 7,238 individuals in the YSRCCYP up to February 2017, with more individuals diagnosed with late cancer onset (n=3,866; 53.4%) compared with early cancer onset (n=3,372; 46.6%). There were more males (n=4,279; 59.1%) than females (n=2,959; 40.9%).

Ethnicity was completed for 77.4% (n= 5,605) of the YSRCCYP, with most individuals classified with white ethnic origin (n=4,987; 68.9%). The second largest ethnicity group was South Asian (n=530; 7.3%). The rest of the cohort with recorded ethnicity were classified as Black (n=28; 0.4%), East Asian (n=29; 0.4%) or other (n=31; 0.4%) (Figure 6.1).

Deprivation group was determined for 94.5% (n=6,840) of the YSRCCYP. Most of the cohort were classified in the most deprived fifth (n=1,748; 24.2%). The second most deprived fifth had the least individuals (n=1,207; 16.7%).

Lymphoma was the most common cancer diagnosis (n=1,485; 20.5%), followed by leukaemias (n=1,382; 19.1%), germ cell tumours (n=1,243; 17.2%) and CNS neoplasms (n=1,225; n=16.9%). After the ‘Other and unspecified’ group, hepatic tumours (n=45; 0.6%), retinoblastomas (n=138; 1.9%) and neuroblastomas (n=187; 2.6%) were the least diagnosed cancer types (Figure 6.1). Apart from lymphomas, germ cell tumours and other malignant epithelial neoplasms, all other cancer types were mostly diagnosed in early onset. No individuals were diagnosed with retinoblastoma in late cancer onset.

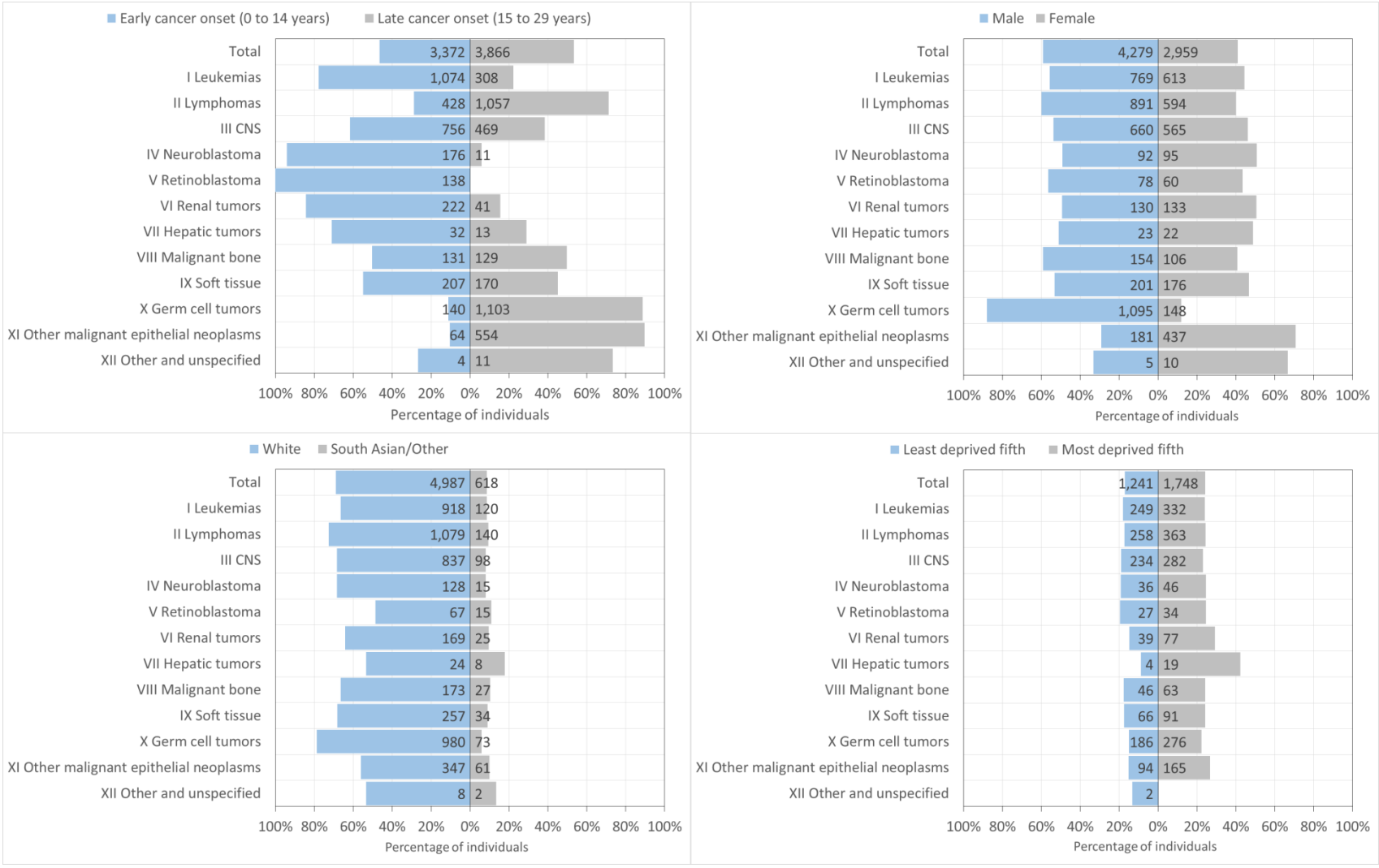


Figure 6.1: Percentage (and number) of individuals by cancer type and socio-demographic groups.

As well as being characterised by late onset, individuals with germ cell tumours were mostly male (n=1,095; 88.1%) and also had the highest proportion with white ethnicity (n=980; 78.8%). The cancer type with the highest proportion of individuals with South Asian/Other ethnicity was hepatic tumours at 17.8% (n=8). Hepatic tumours also had the highest proportion of individuals resident in the most deprived fifth (n=19; 42.2%). The most deprived fifth had the highest percentage of individuals for all cancer types.

6.3.2 Mental health admissions data analysis.

6.3.2.1 Demographics.

A total of 602 individuals in the YSRCCYP (8.3%) had a mental health admission recorded either on the MHMDS or on the HES inpatient data. There were more individuals with a mental health admission who had late cancer onset (n=372; 61.8%) compared with early cancer onset (n=230; 38.2%). More males (n=348; 57.8%) than females (n=254; 42.4%) and more individuals with white ethnicity (n=471; 78.2%) compared with South Asian/Other ethnicity (n=40; 6.6%) had a mental health admission. The most deprived fifth had the highest total of individuals with a mental health admission (n=192; 31.9%) and had over two and a half times the total of the least deprived fifth, which had the lowest total of individuals (n=75; 12.5%).

Most individuals with late cancer onset who had a mental health admission were diagnosed with lymphomas (n=101; 77.1%) or germ cell tumours (n=107; 92.2%). CNS neoplasms and lymphomas had slightly more males with a mental health admission compared with females. However, for germ cell tumours, the percentage of males with a mental health admission was around 90%.

The first known recorded mental health admission mostly occurred during the transitional care period (n=318; 53%) and after cancer diagnosis (n=508; 84.4%) (Figure 6.2). Two thirds of individuals had their first mental health admission during the follow-up period at least 5 years after their initial cancer diagnosis (n=399; 66.3%).

Figure 6.2: Percentage (and number) of individuals with a mental health admission by socio-demographic groups, cancer type and time since cancer diagnosis.

6.3.2.2 Incidence rates for mental health admissions.

Incidence for first known mental health admission was 6.6 per 1,000 person-years (95% CI 6.1 to 7.1 per 1,000 person-years) for the overall cohort, 4.5 per 1,000 person-years (95% CI 4.0 to 5.1 per 1,000 person-years) in early cancer onset (Figure 6.3) and 9.2 per 1,000 person-years (95% CI 8.3 to 10.2 per 1,000 person-years) in late cancer onset (Figure 6.4). No significant differences in incidence rates were found by sex, ethnicity and cancer type and there were increasing trends in first mental health admission from the 'Least deprived fifth' to the 'Most deprived fifth'.

Both onset groups had an increasing trend in incidence by 5-year age group. However, in early cancer onset there is a five-fold increase in incidence from the 15 to 19 year age group to the 20 to 24 year age group (Figure 6.3).

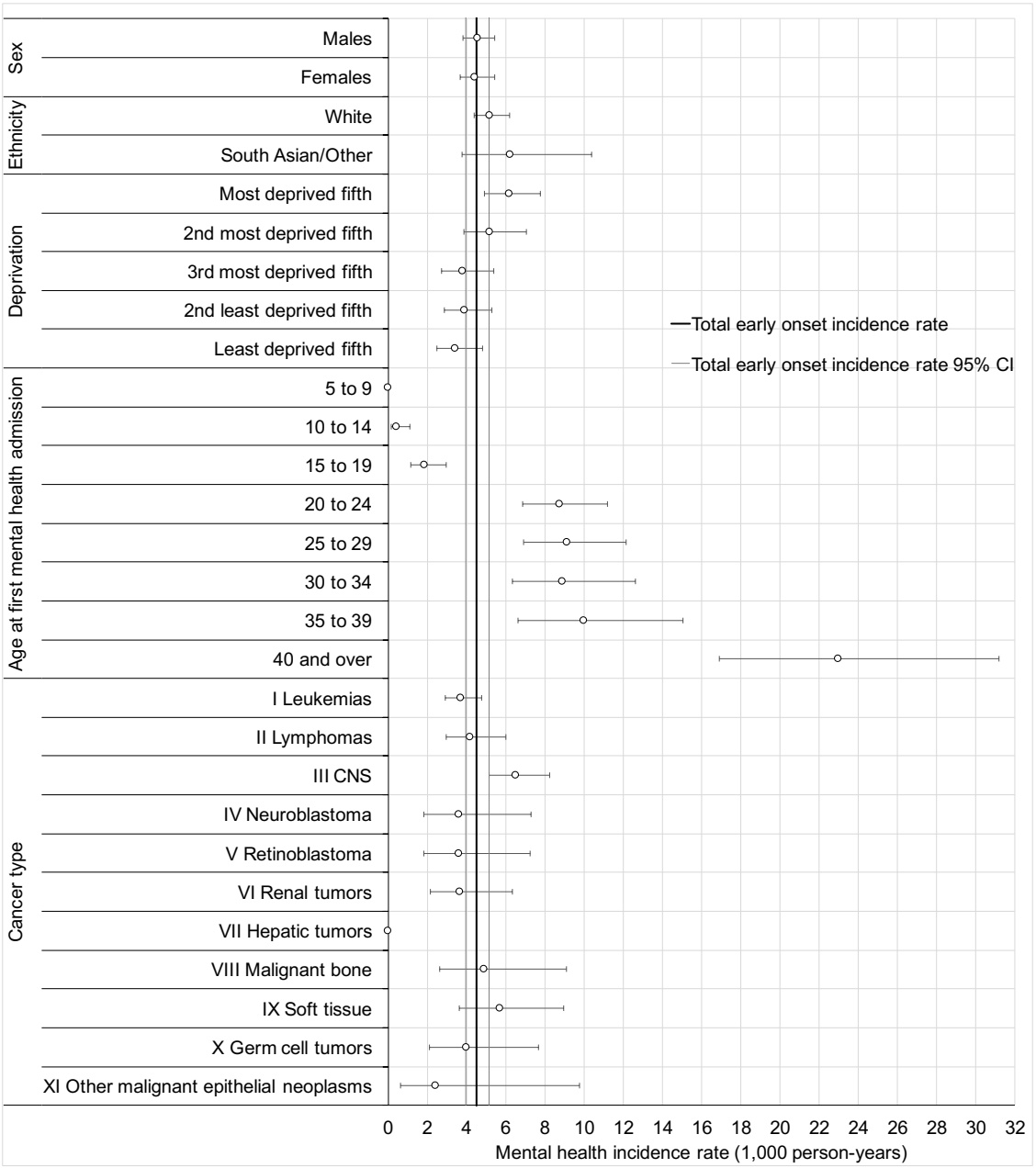


Figure 6.3: Incidence rate per 1,000 person-years for mental health incidence - early cancer onset.

This increase in incidence for the same age groups was less pronounced in late cancer onset, where there was an increase of around 60% from the 15 to 19-year age group to the 20 to 24-year group, although there was no statistically significant difference between the groups in late onset (Figure 6.4).

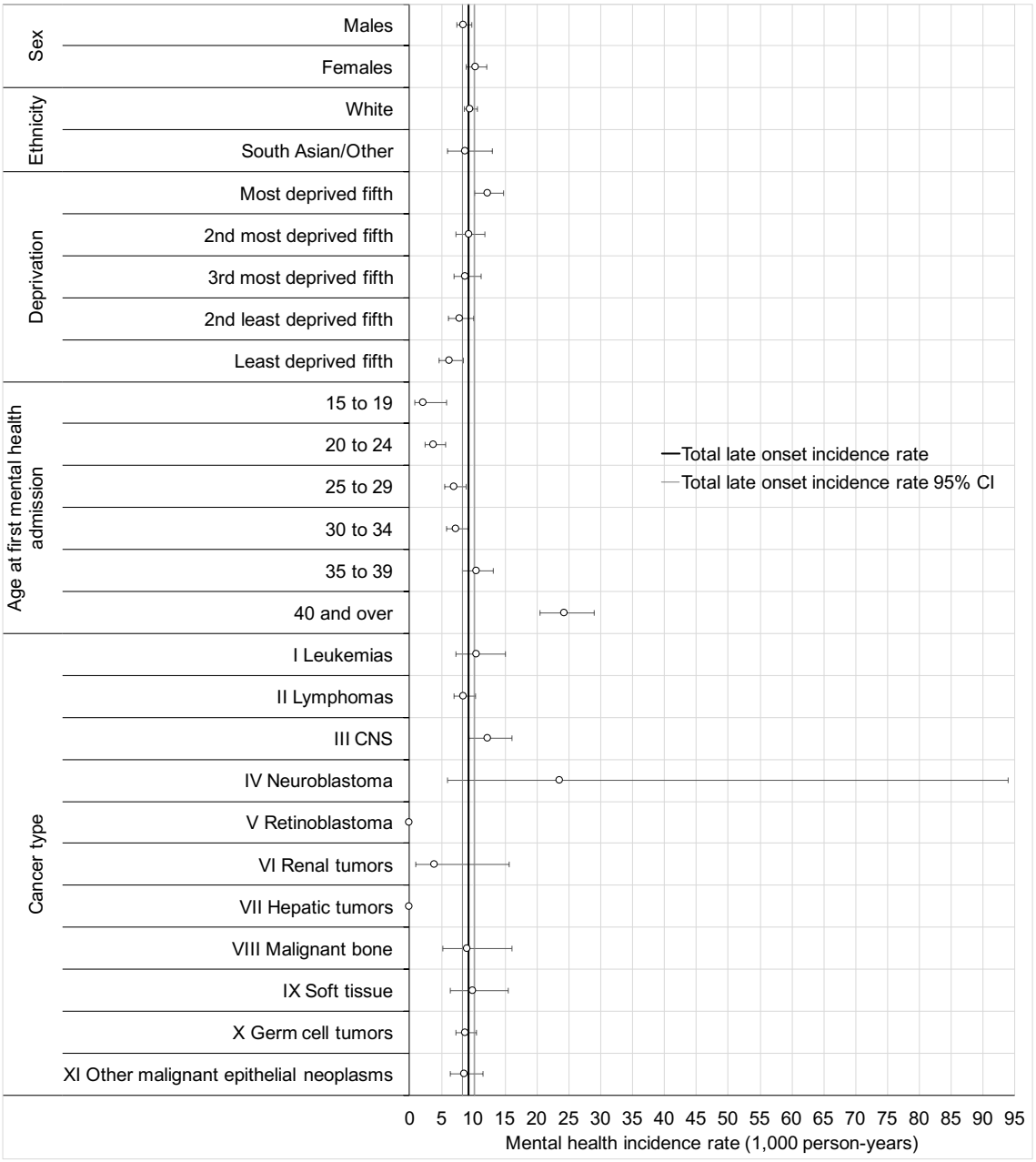


Figure 6.4 : Incidence rate per 1,000 person-years for mental health incidence – late cancer onset.

6.3.2.3 Mental health and age at first mental health admission.

There were no significant differences in risk of mental health admission by age groups compared with the 10 to 14-year age group in early cancer onset (Figure 6.5). However, there were significant differences by age groups found in late cancer onset. Compared with the 40 years and over age group, the age groups between 20 to 39 years had significantly higher risk of first mental health admission, with the highest risk in the 25 to 29-year age group at 2.07 (95% CI 1.6 to 2.68) (Figure 6.6).

There were also differences between the onset groups by sex. There was a significantly lower risk of a mental health admission in females compared with males in late cancer onset by around 40% (Figure 6.6). In early onset, females had a lower risk of a mental health admission compared with males by around 20%, although this was not significantly different (Figure 6.5).

Both onset groups showed no significant differences in risk of mental health admission by ethnicity or deprivation groups.

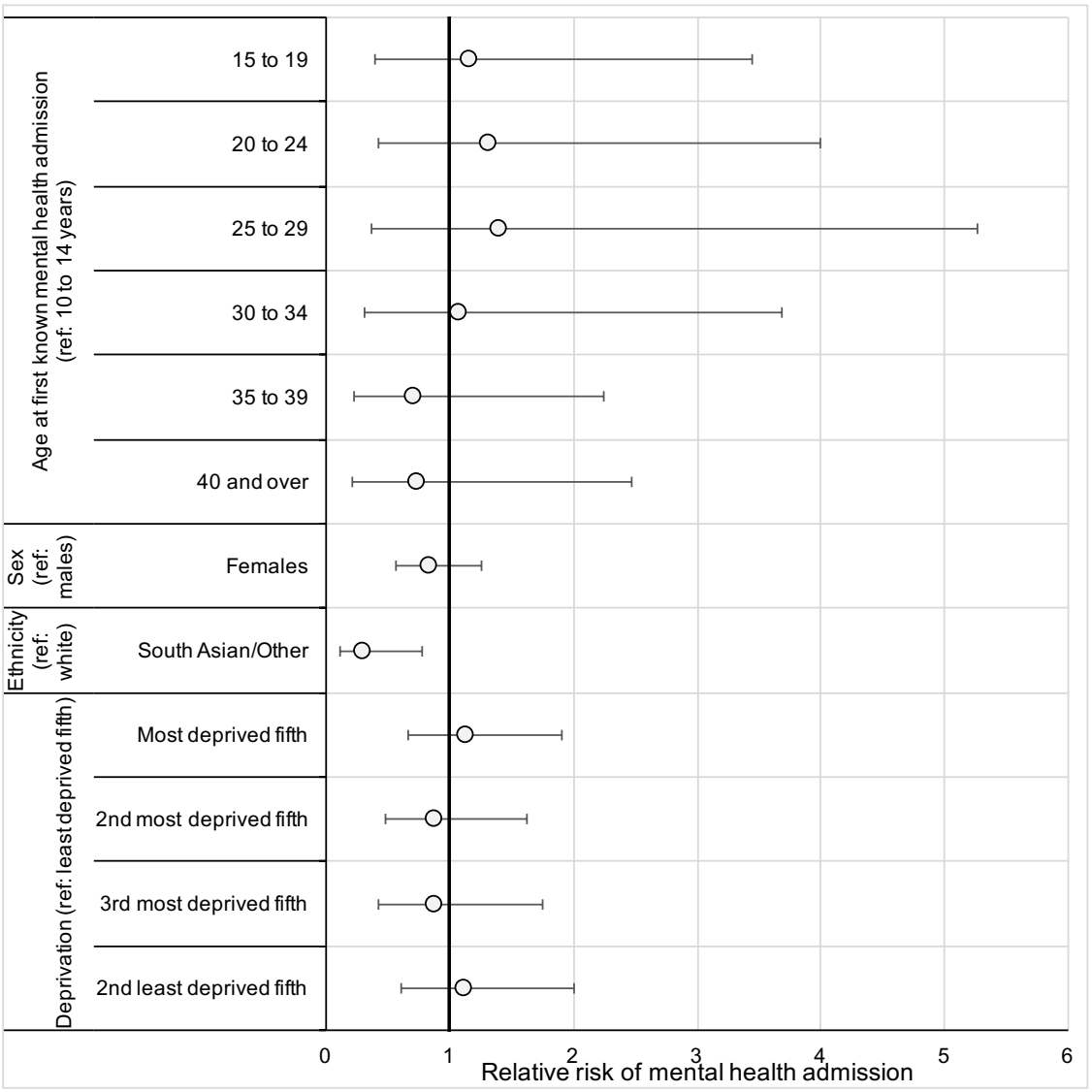


Figure 6.5: Relative risk from Poisson model with 95% confidence intervals by age at first mental health admission – early cancer onset with a mental health admission.

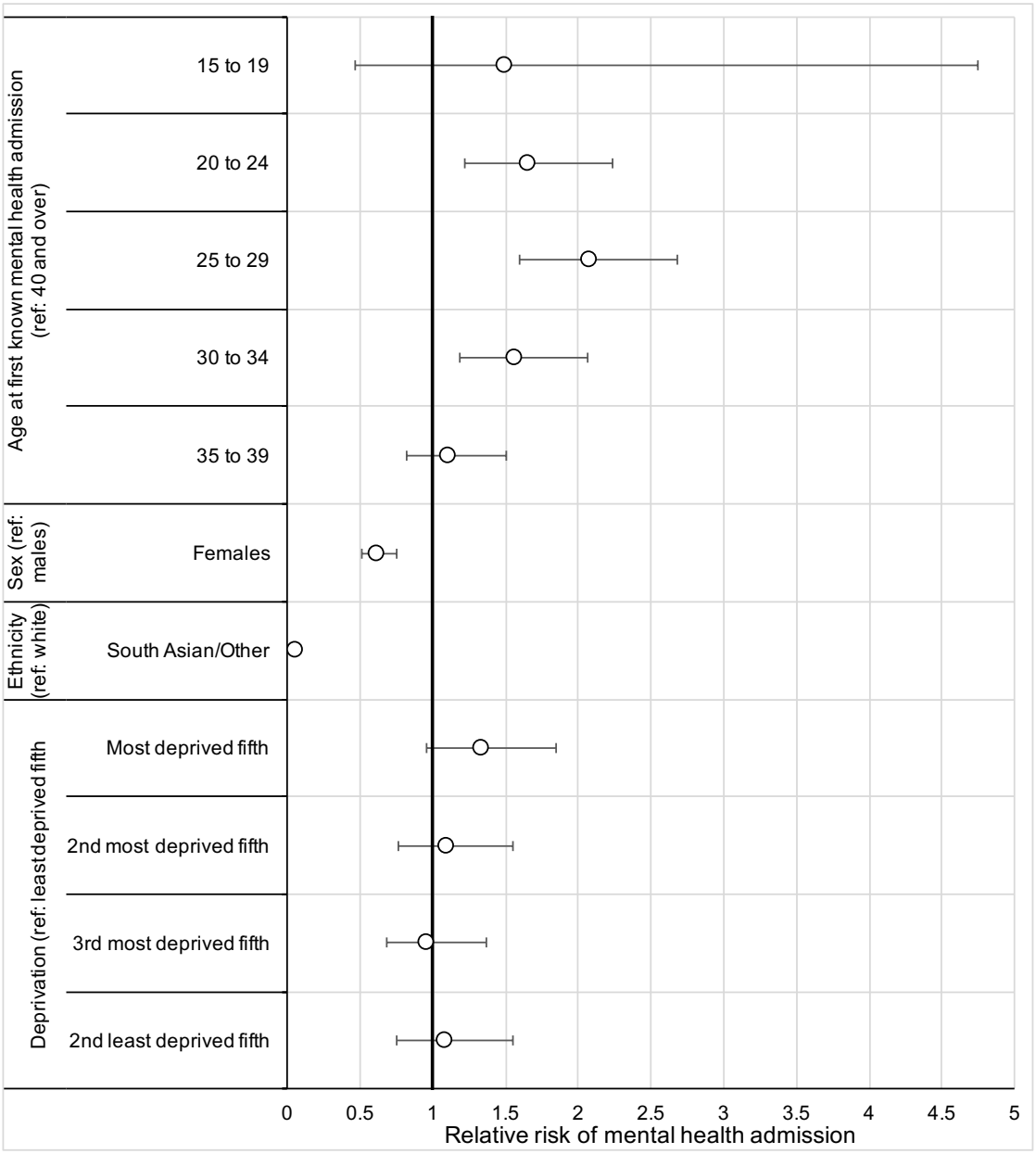


Figure 6.6: Relative risk from Poisson model with 95% confidence intervals by age at first mental health admission – late cancer onset with a mental health admission.

6.3.2.4 Mental health by cancer type.

Leukaemias, lymphomas and CNS neoplasms all had significantly higher risk of mental health admission compared with the reference cancer types in early and late cancer onset. Lymphomas had the largest relative risk in early onset at 7.6 (95% CI 3.7 to 15.61). In late cancer onset, germ cell tumours had the largest relative risk of a first mental health admission compared with neuroblastoma with a relative risk of 6.36 (95% CI 3.62 to 11.17).

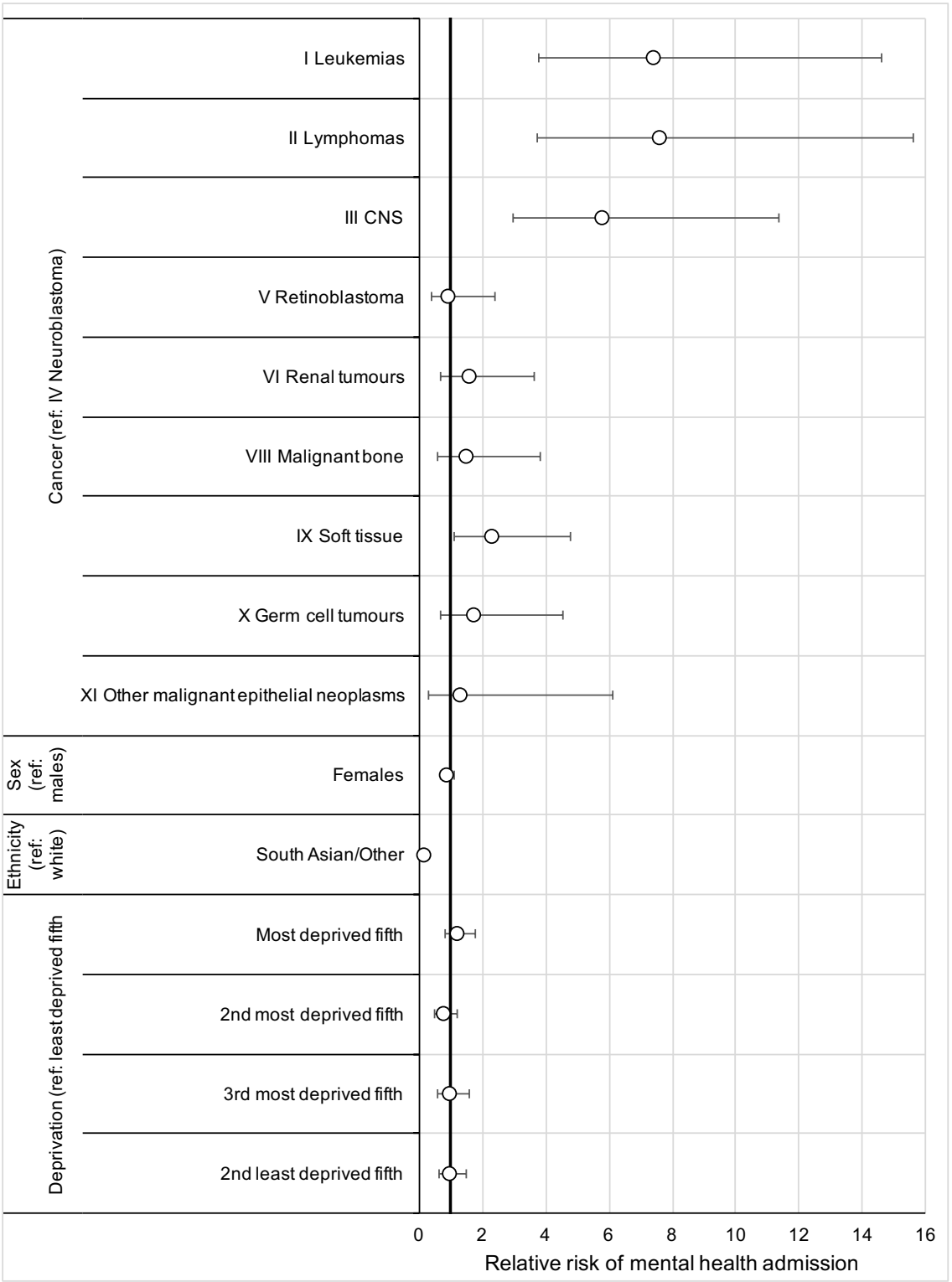


Figure 6.7: Relative risk from Poisson model with 95% confidence intervals by cancer type – early cancer onset with a mental health admission.

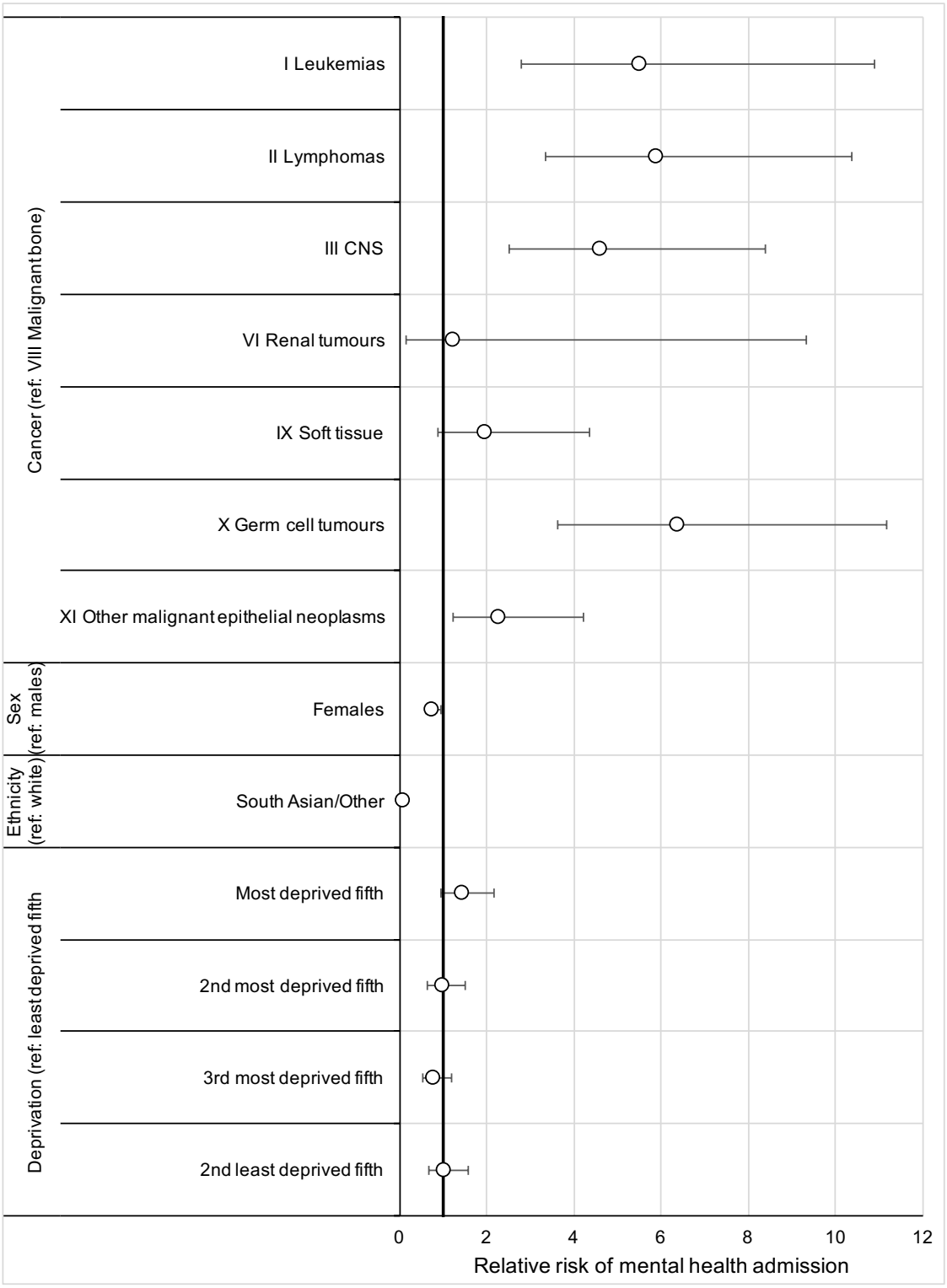


Figure 6.8: Relative risk from Poisson model with 95% confidence intervals by cancer type – late cancer onset with a mental health admission.

6.3.3 Outpatient appointment data analysis.

6.3.3.1 Demographics.

There were 4,735 individuals in the YSRCCYP matched to the outpatient HES dataset. Percentages of individuals with an outpatient appointment by all socio-demographic categories were similar to the percentages of the overall YSRCCYP cohort, apart from ethnicity where the percentage of individuals with an outpatient appointment with white ethnic origin was slightly higher at 79.0% (Figure 6.9), compared with 68.9% in the overall YSRCCYP cohort (Figure 6.1).

Of the 4,735 individuals matched to the outpatient data, 1,837 (38.3%) attended all their outpatient appointments. Therefore, the majority of individuals (61.2%) had at least one outpatient appointment with a DNA status (Table 6.3). For South Asian/Other ethnicity, the percentage of individuals with at least one DNA status was slightly higher at 67.3%. There were also differences between deprivation groups where the least deprived fifth had the lowest percentage at of at least one DNA appointment at 54.6%, compared with the most deprived group at 69.4%.

By cancer type, after the ‘Other and unspecified’ group, retinoblastoma (70%), other malignant epithelial neoplasms (66.2%) and malignant bone tumours (65.5%) had the highest percentages of individuals with at least one DNA outpatient appointment. The cancer types with the lowest percentages of DNA outpatient appointments were germ cell tumours (55.3%), lymphomas (60.4%), CNS neoplasms (60.8%), soft tissue tumours (62.2%), neuroblastomas (62.2%) and leukaemias (62.6%).

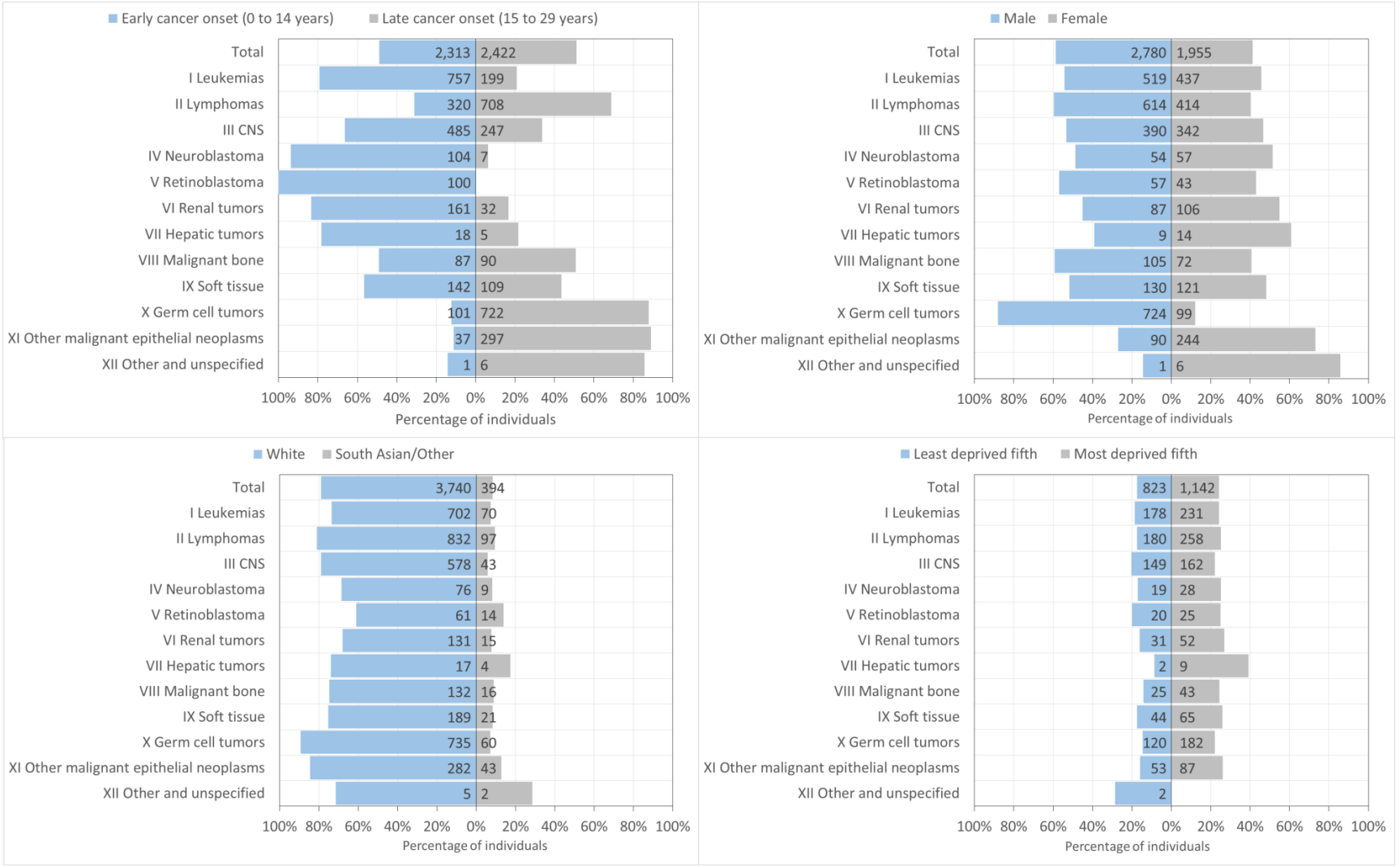


Figure 6.9: Percentage (and number) of individuals linked to outpatient data by cancer type and socio-demographic groups.

Table 6.3: Number of individuals linked to outpatient data by attended status, socio-demographic groups and cancer type.

		Individuals with at least one outpatient appointment with a DNA status		Individuals with no outpatient appointments with a DNA status		Total individuals
		N	%	N	%	
Age at cancer diagnosis	0 to 15 years (early onset)	1,433	62.0	880	38.0	2,313
	15 to 29 years (late onset)	1,465	60.5	957	39.5	2,422
Sex	Males	1,671	60.1	1,109	39.9	2,780
	Females	1,227	62.8	728	37.2	1,955
Ethnicity	White	2,279	60.9	1,461	39.1	3,740
	South Asian/Other	265	67.3	129	32.7	394
Deprivation	Least deprived fifth	449	54.6	374	45.4	823
	2nd least deprived fifth	503	54.3	424	45.7	927
	3rd most deprived fifth	518	62.5	311	37.5	829
	2nd most deprived fifth	522	64.0	293	36.0	815
	Most deprived fifth	792	69.4	350	30.6	1,142
Cancer type	I Leukaemias	598	62.6	358	37.4	956
	II Lymphomas	621	60.4	407	39.6	1,028
	III CNS	445	60.8	287	39.2	732
	IV Neuroblastoma	69	62.2	42	37.8	111

	V Retinoblastoma	70	70.0	30	30.0	100
	VI Renal tumours	126	65.3	67	34.7	193
	VII Hepatic tumours	15	65.2	8	34.8	23
	VIII Malignant bone	116	65.5	61	34.5	177
	IX Soft tissue	156	62.2	95	37.8	251
	X Germ cell tumours	455	55.3	368	44.7	823
	XI Other malignant epithelial neoplasms	221	66.2	113	33.8	334
Total		2,898	61.2	1,837	38.8	4,735

6.3.3.2 Total outpatient appointments by socio-demographic groups, cancer type and treatment specialty.

There were 122,422 outpatient appointments, with a median of 16 (range 1 to 369) appointments per individual. Around 10% of all outpatient appointments had a DNA status. There was a median of 3 (range 1 to 74) DNA appointments per individual (Table 6.4).

There were more outpatient appointments for early cancer onset (57.6%) compared with late onset (42.4%). With more appointments in the early onset group, the median number of appointments per individual was higher by around 7 appointments compared with the late onset group (Table 6.4). The percentage of outpatient appointments with DNA status was around 2% higher in the late cancer onset group compared with the early onset group.

Although there were 17.4% more males with an outpatient appointment compared with females (Figure 6.9), the total of outpatient appointments was evenly split between the sexes (48.9% for males vs. 51.1% for females). Females had a higher median appointment per individual by 10 compared with males, although the percentage of outpatient appointments with DNA status was around 2% higher in males compared with females (Table 6.4).

There were around three times more outpatient appointments with DNA status in the most deprived fifth (n=4,032) compared with the least deprived fifth (n= 1,621). There was only a slight difference in median DNA appointments of 1 per individual between the most and least deprived fifths (Table 6.4).

There was a total of 20,740 (16.9%) outpatient appointments before, 50,484 (41.2%) during and 51,198 (41.8%) after the transitional care period. The percentage of appointments with a DNA status before the transitional care period was lower (8%; n=1,666) compared with during (11.1%; n=5,622) and after the transitional care period (10.4%; n=5,303). For 5-year age bands, the 30 to 34-year age group had the highest number of DNA appointments, followed by the 25 to 29-year group. Mean DNA appointment per individual ranged between 2.7 to 3.3 for all age groups (Table 6.4).

The highest number of outpatient appointments took place within the oncology treatment specialty (n=33,831; 27.6%). With the exception of retinoblastoma and hepatic tumours, the majority of outpatient appointments in all other cancer types were classified within the oncology treatment specialty. There were no mental health appointments for hepatic tumours (Table 6.5). After the other/unknown category, mental health, digestion and endocrinology had the highest percentage of DNA appointments.

Table 6.4: Descriptive statistics of outpatient appointments by socio-demographic groups and age at outpatient appointment.

		Total outpatient appointments					Total outpatient appointments with DNA status					
		N	% of total	Mean	Median (range)	Standard deviation	N	% of total	% within group	Mean	Median (range)	Standard deviation
Age at cancer diagnosis	0 to 14 years (early onset)	70,476	57.6	30.5	19 (1 to 327)	33.8	6,635	52.7	9.4	4.7	3 (1 to 74)	5.8
	15 to 29 years (late onset)	51,946	42.4	21.4	12 (1 to 369)	26.2	5,956	47.3	11.5	4.1	2 (1 to 50)	4.6
Sex	Males	59,814	48.9	21.5	12 (1 to 369)	27.5	6,732	53.5	11.3	4.1	2 (1 to 74)	5.1
	Females	62,608	51.1	32.0	22 (1 to 286)	33.3	5,859	46.5	9.4	4.8	3 (1 to 48)	5.4
Ethnicity	White	95,015	77.6	25.4	15 (1 to 369)	30.1	9,719	77.2	10.2	4.3	2 (1 to 74)	5.2
	South Asian/Other	9,650	7.9	24.5	14 (1 to 148)	27.7	1,206	9.6	12.5	4.6	3 (1 to 34)	4.7
Deprivation	Least deprived fifth	21,135	17.3	25.7	15 (1 to 221)	30.0	1,621	12.9	7.7	3.6	2 (1 to 37)	4.1
	2nd least deprived fifth	23,612	19.3	25.5	15 (1 to 327)	31.3	1,885	15.0	8.0	3.8	2 (1 to 66)	5.2
	3rd most deprived fifth	20,564	16.8	24.8	15 (1 to 261)	28.9	2,053	16.3	10.0	4.0	3 (1 to 34)	4.2
	2nd most deprived fifth	22,564	18.4	27.7	18 (1 to 369)	32.3	2,495	19.8	11.1	4.8	3 (1 to 47)	5.3
	Most deprived fifth	29,955	24.5	26.2	16 (1 to 314)	29.9	4,032	32.0	13.5	5.1	3 (1 to 74)	6.2
Age at outpatient appointment	5 to 9	7,027	5.7	11.8	6 (1 to 126)	15.8	642	5.1	9.1	3.2	2 (1 to 34)	4.0
	10 to 14	13,713	11.2	14.5	9 (1 to 157)	17.3	1,024	8.1	7.5	3.0	2 (1 to 31)	3.2
	15 to 19	15,938	13.0	13.4	8 (1 to 181)	17.2	1,564	12.4	9.8	3.1	2 (1 to 25)	3.1
	20 to 24	15,230	12.4	10.9	6 (1 to 98)	12.9	1,855	14.7	12.2	2.9	2 (1 to 36)	3.0
	25 to 29	19,316	15.8	11.5	6 (1 to 159)	15.8	2,203	17.5	11.4	2.8	2 (1 to 34)	3.2
	30 to 34	21,411	17.5	10.6	6 (1 to 153)	13.9	2,317	18.4	10.8	2.7	2 (1 to 22)	2.6
	35 to 39	17,240	14.1	11.7	7 (1 to 181)	15.6	1,823	14.5	10.6	2.8	2 (1 to 45)	3.2
	40 and over	12,547	10.2	14.6	8 (1 to 164)	19.9	1,163	9.2	9.3	3.3	2 (1 to 29)	4.0
Total		122,422	100.0	25.9	16 (1 to 369)	30.5	12,591	100.0	10.3	4.4	3 (1 to 74)	5.3

Table 6.5: Number of outpatient appointments by treatment specialty and cancer type.

	I Leukaemias		II Lymphomas		III CNS		IV Neuroblastoma		V Retinoblastoma	
	N	%	N	%	N	%	N	%	N	%
Circulatory	1,020	3.7	550	2.3	216	0.8	67	2.1	17	0.6
Digestion	686	2.5	510	2.2	377	1.5	43	1.4	31	1.2
Ears/Nose/ Throat	873	3.1	758	3.2	1,161	4.5	246	7.8	93	3.5
Endocrinology	1,787	6.4	659	2.8	2,871	11.1	**269**	**8.6**	15	0.6
Eyes	997	3.6	488	2.1	**2,931**	**11.3**	106	3.4	**1,086**	**40.3**
Joints/Muscles/Skin	**2,678**	**9.6**	**2,769**	**11.8**	2,194	8.5	**417**	**13.3**	**184**	**6.8**
Maternity/Obstetrics/ Gynaecology	**1,948**	**7.0**	**2,636**	**11.2**	1,000	3.9	177	5.6	130	4.8
Mental health	265	1.0	223	0.9	712	2.8	24	0.8	43	1.6
Nephrology	554	2.0	446	1.9	358	1.4	83	2.6	8	0.3
Neurology	651	2.3	357	1.5	**4,392**	**17.0**	101	3.2	48	1.8
Oncology	**10,541**	**37.8**	**8,984**	**38.2**	**4,403**	**17.0**	**552**	**17.5**	**486**	**18.0**
Oral health	1,066	3.8	765	3.3	752	2.9	179	5.7	159	5.9
Respiratory	270	1.0	346	1.5	217	0.8	83	2.6	7	0.3
Surgery	858	3.1	1,904	8.1	851	3.3	138	4.4	80	3.0
Total	27,876	100.0	23,502	100.0	25,833	100.0	3,146	100.0	2,693	100.0

Figures in **bold** represent the 3 treatment specialties with the highest total of outpatient appointments within the cancer type category.

Table 6.5 continued: Number of outpatient appointments by treatment specialty and cancer type.

	VI Renal tumours		VII Hepatic tumours		VIII Malignant bone		IX Soft tissue		X Germ cell tumours		XI Other malignant epithelial neoplasms	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Circulatory	222	4.2	9	1.8	237	4.7	275	3.9	364	3.0	83	0.9
Digestion	146	2.8	**117**	**22.8**	87	1.7	171	2.4	345	2.8	338	3.8
Ears/Nose/ Throat	278	5.3	45	8.8	158	3.1	300	4.2	365	3.0	691	7.8
Endocrinology	140	2.7	-	-	170	3.3	413	5.8	773	6.4	**1,070**	**12.1**
Eyes	228	4.3	9	1.8	176	3.5	309	4.3	534	4.4	404	4.6
Joints/Muscles/ Skin	364	6.9	**53**	**10.3**	**921**	**18.1**	637	8.9	**1,885**	**15.5**	726	8.2
Maternity/ Obstetrics/ Gynaecology	**504**	**9.6**	28	5.4	**468**	**9.2**	**760**	**10.7**	853	7.0	**1,292**	**14.7**
Mental health	53	1.0	-	-	50	1.0	84	1.2	318	2.6	54	0.6
Nephrology	**806**	**15.4**	4	0.8	182	3.6	358	5.0	**877**	**7.2**	241	2.7
Neurology	88	1.7	8	1.6	78	1.5	189	2.6	534	4.4	179	2.0
Oncology	**1,215**	**23.1**	**103**	**20.0**	**1,487**	**29.2**	**1,406**	**19.7**	**2,880**	**23.7**	**1,641**	**18.6**
Oral health	154	2.9	20	3.9	161	3.2	566	7.9	329	2.7	458	5.2
Respiratory	86	1.6	2	0.4	78	1.5	124	1.7	181	1.5	67	0.8
Surgery	307	5.8	24	4.7	233	4.6	**654**	**9.2**	864	7.1	824	9.3
Total	5,250	100.0	514	100.0	5,089	100.0	7,134	100.0	12,172	100.0	8,817	100.0

Figures in **bold** represent the 3 treatment specialities with the highest total of outpatient appointments within the cancer type category.

6.3.3.3 Incidence rates for outpatient appointments with a ‘did not attend’ (DNA) status.

The overall incidence rate of DNA appointments in the YSRCCYP was 391.2 per 1,000 person-years (95% CI 384.5 to 398.1 per 1,000 person-years). The incidence rate of DNA appointments in early cancer onset was significantly lower than in late cancer onset (312 per 1,000 person-years (95% CI 304.6 to 319.6 per 1,000 person-years) vs. 545.6 per 1,000 person-years (95% CI 531.9 to 559.6 per 1,000 person-years)) (Figure 6.10; Figure 6.11).

In both early and late cancer onset, females had significantly higher incidence rates of DNA appointments compared with males. South Asian/Other ethnicity also had significantly higher incidence rates of about 50% compared with white ethnicity (unknown ethnicity was 135 per 1,000 person-years (95% CI 128 to 141 per 1,000 person-years) in early cancer onset and 189 per 1,000 person-years (95% CI 98 to 363 per 1,000 person-years) in late cancer onset). Incidence rates of DNA appointments by deprivation groups showed decreasing rates from the ‘Most deprived’ group to the ‘Least deprived’. The two most deprived groups had significantly higher DNA incidence rate compared with the overall rate and three least deprived groups (Figure 6.10; Figure 6.11).

For early cancer onset, there was an increasing incidence rate by age group from the 10 to 14-year age group which was the only age group to have significantly lower incidence compared with the overall early cancer onset incidence. The 30 to 34 and 35 to 39-year age groups had significantly higher incidence rates compared with the overall early onset incidence (Figure 6.10). In late cancer onset, there was a decreasing trend in incidence rate up to the 40 and over age group which had the highest DNA appointment incidence rate and was the only age group with a significantly higher incidence rate compared with the overall late onset incidence rate (Figure 6.11).

In early cancer onset, lymphomas had significantly lower incidence of DNA appointments and retinoblastoma, germ cells and other malignant epithelial had significantly higher incidence compared with the overall early onset rate (Figure 6.10). In late cancer onset, CNS, hepatic, malignant bone, soft tissue and germ cell tumours had significantly lower incidence of DNAs and leukaemias, lymphomas, renal tumours and other malignant epithelial neoplasms had significantly higher incidences of DNAs compared with the overall late onset cohort (Figure 6.11).

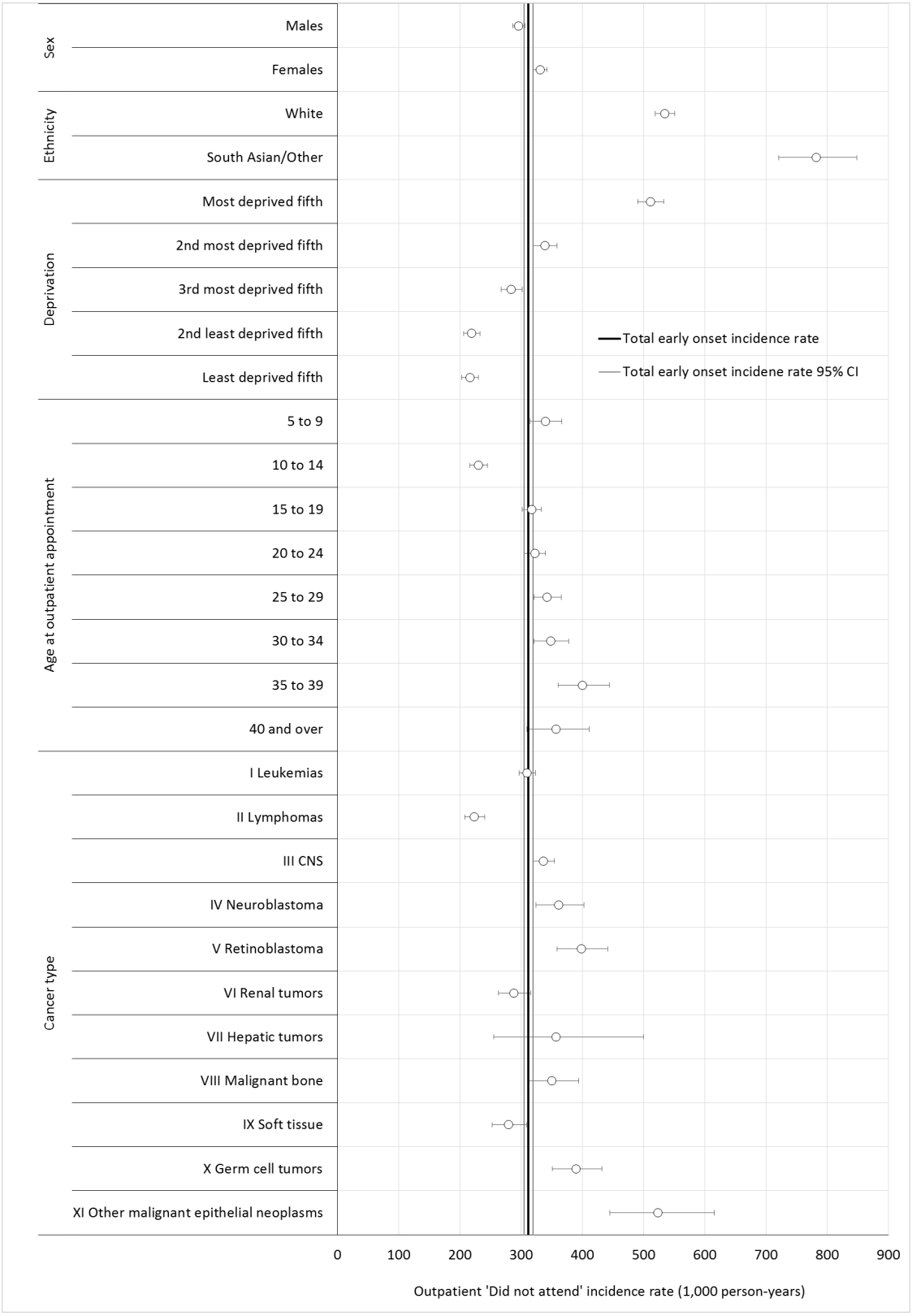


Figure 6.10: Incidence rate per 1,000 person-years for outpatient appointments with 'did not attend' (DNA) status - early onset group.

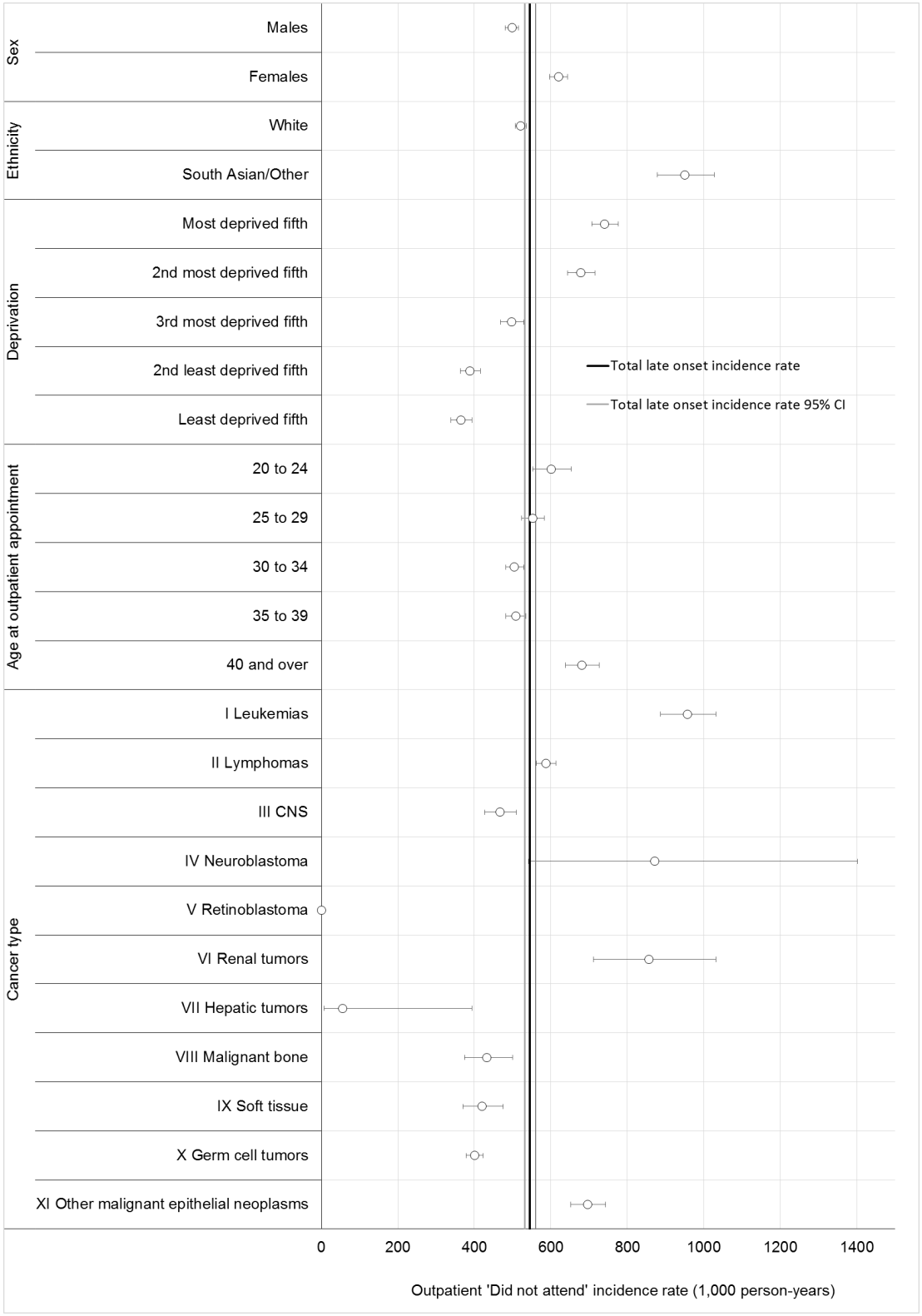


Figure 6.11: Incidence rate per 1,000 person-years for outpatient appointments with 'did not attend' (DNA) status - early onset group.

6.3.3.4 Outpatient appointments by age at outpatient appointment.

Mixed effects logistic regression modelling was used to assess odds of a DNA outpatient appointment by age at outpatient appointment. For the sensitivity

analysis, models were run only for individuals matched on the outpatient dataset who were diagnosed since 1st April 1998.

In early cancer onset, all age groups at outpatient appointment, apart from the 5 to 9 age group, had a significantly higher odds of a DNA outpatient appointment compared with the 10 to 14-year age group. During the transitional care period, the odds of a DNA appointment was significantly lower in the 15 to 19-year age group, compared with the 20 to 24 and 25 to 29-year age groups. After the transitional care period, there was a decreasing trend in odds from the 35 to 39-year age group (Figure 6.12).

In late cancer onset, no significant differences were found in odds of a DNA outpatient appointment with any age groups (Figure 6.13). Similar trends were found in the equivalent sensitivity cohorts, although the odds of a DNA appointment in the 25 to 29-year age group in early cancer onset was more than double that in the total cohort at 5.82 (95% CI 4.28 to 7.93) and the wide 95% confidence intervals for the 30 to 34-year age group meant that the odds were no longer significantly different compared with the 10 to 14-year age group.

Females were found to have a significantly lower odds of an outpatient appointment with a DNA status compared with males both in early (Figure 6.12) and late cancer onset (Figure 6.13). The odds of females not attending an outpatient appointment compared with males was significantly lower in late cancer onset (0.61 (95% CI 0.54 to 0.70)) compared with early cancer onset (0.84 (95% CI 0.73 to 0.95). Odds ratios for females were similar in all equivalent sensitivity cohorts.

Individuals in the three most deprived fifths had significantly higher odds of a DNA outpatient appointment compared with individuals in the least deprived groups in both early (Figure 6.12) and late cancer onset (Figure 6.13). There were no significant differences in odds between the 2nd least deprived fifth compared with the least deprived fifth. The sensitivity cohorts found similar decreasing trends in odds with decreasing deprivation. However, in early cancer onset only the most deprived fifth had a significantly higher odds of a DNA appointment compared with the least deprived fifth and in late onset, only the two most deprived groups had significantly higher odds of a DNA appointment compared with the least deprived fifth.

In both early (Figure 6.12) and late cancer onset (Figure 6.13), there were no significant differences in DNA outpatient appointments between South Asian/Other ethnicity and white ethnicity.

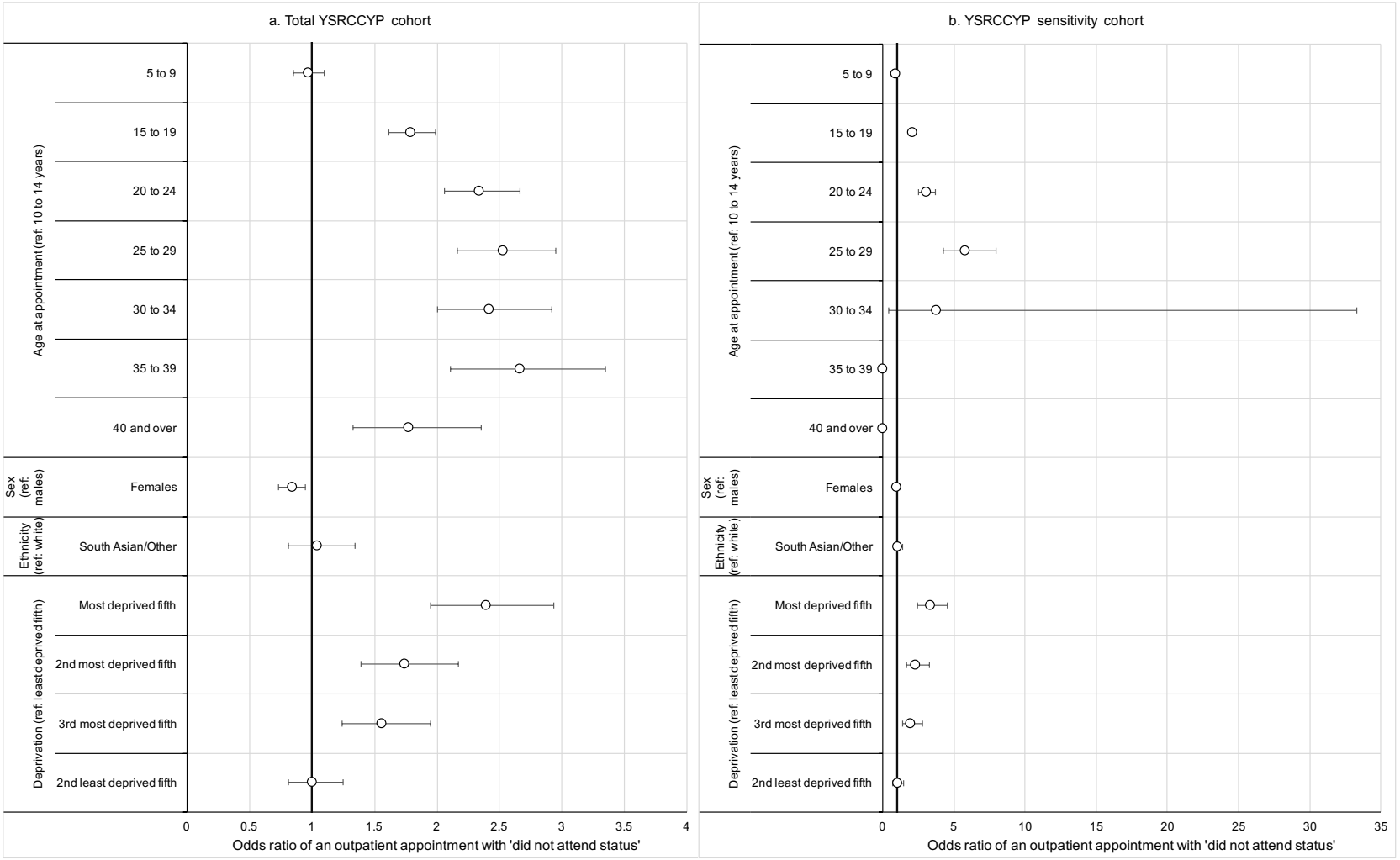


Figure 6.12: Odds ratios of 'did not attend' (DNA) status from mixed effects logistic regression model with 95% confidence intervals by age at appointment – early cancer onset (a.) and equivalent sensitivity cohort (b.).

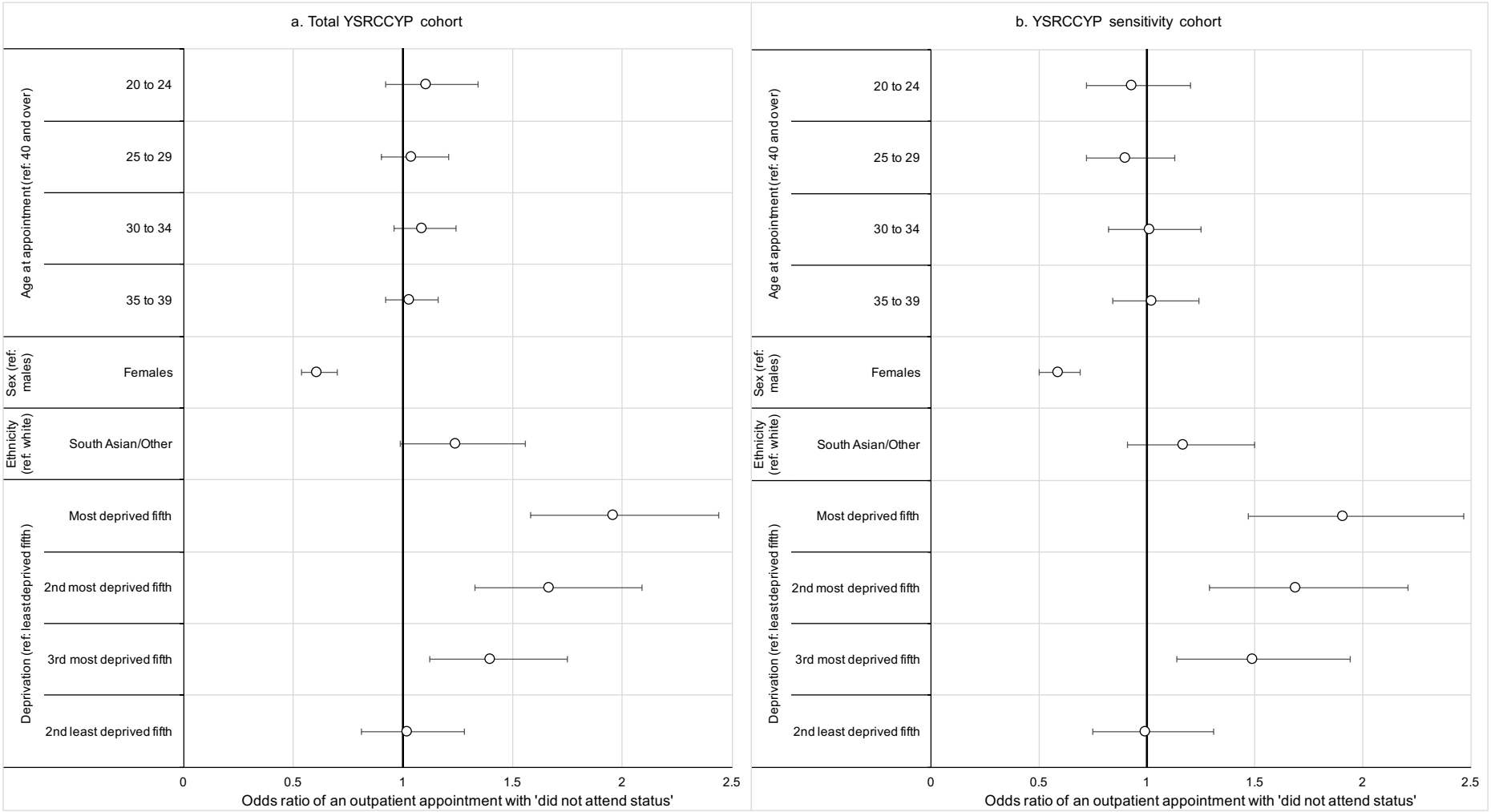


Figure 6.13: Odds ratios of 'did not attend' (DNA) status from mixed effects logistic regression model with 95% confidence intervals by age at appointment – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.3.5 Outpatient appointments by cancer type.

The mixed effects logistic regressions models by cancer type showed similar results by socio-demographic groups to the age at outpatient appointment models in early and late cancer onset.

For early cancer onset, individuals diagnosed with CNS neoplasms (0.67; 95% CI 0.48 to 0.93) had a significantly lower odds of DNA appointments compared with individuals diagnosed with neuroblastomas. All other cancer types had no significant difference in odds of a DNA appointment compared with neuroblastoma. This was also found for the sensitivity cohort (Figure 6.14).

In late cancer onset, compared with malignant bone tumours, lymphomas (1.82; 95% CI 1.24 to 2.68), renal tumours (1.96; 95% CI 1.03 to 3.71), germ cell tumours (1.63; 95% CI 1.14 to 2.32) and other malignant epithelial neoplasms (1.8; 95% CI 1.23 to 2.62) had significantly higher odds of a DNA outpatient appointment. However, no cancer types in the sensitivity cohort showed any significant differences of odds for a DNA appointment compared with malignant bone tumours (Figure 6.15).

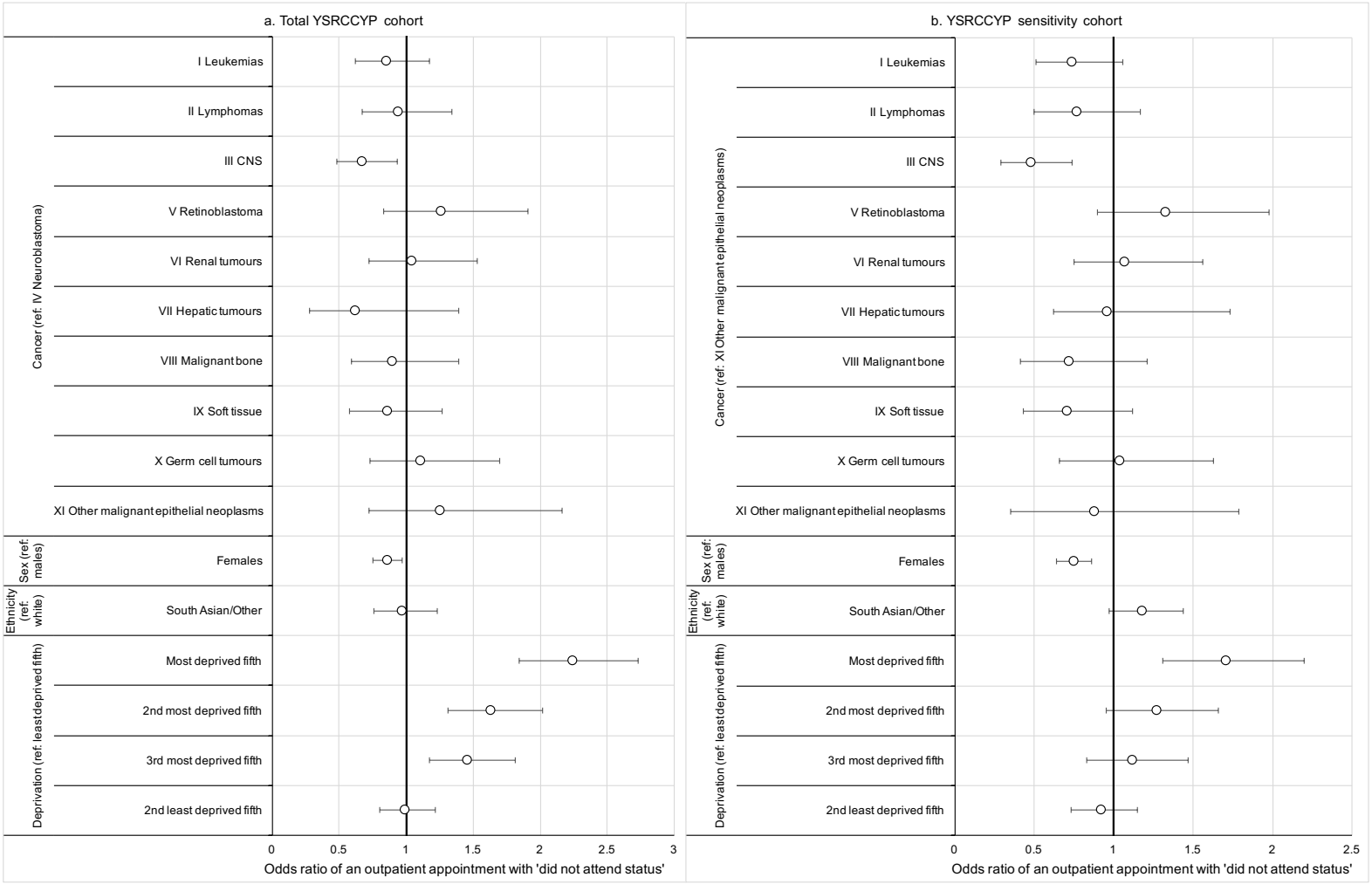


Figure 6.14: Odds ratios of 'did not attend' (DNA) status from mixed effects logistic regression model with 95% confidence intervals by cancer type – early cancer onset (a.) and equivalent sensitivity cohort (b.).

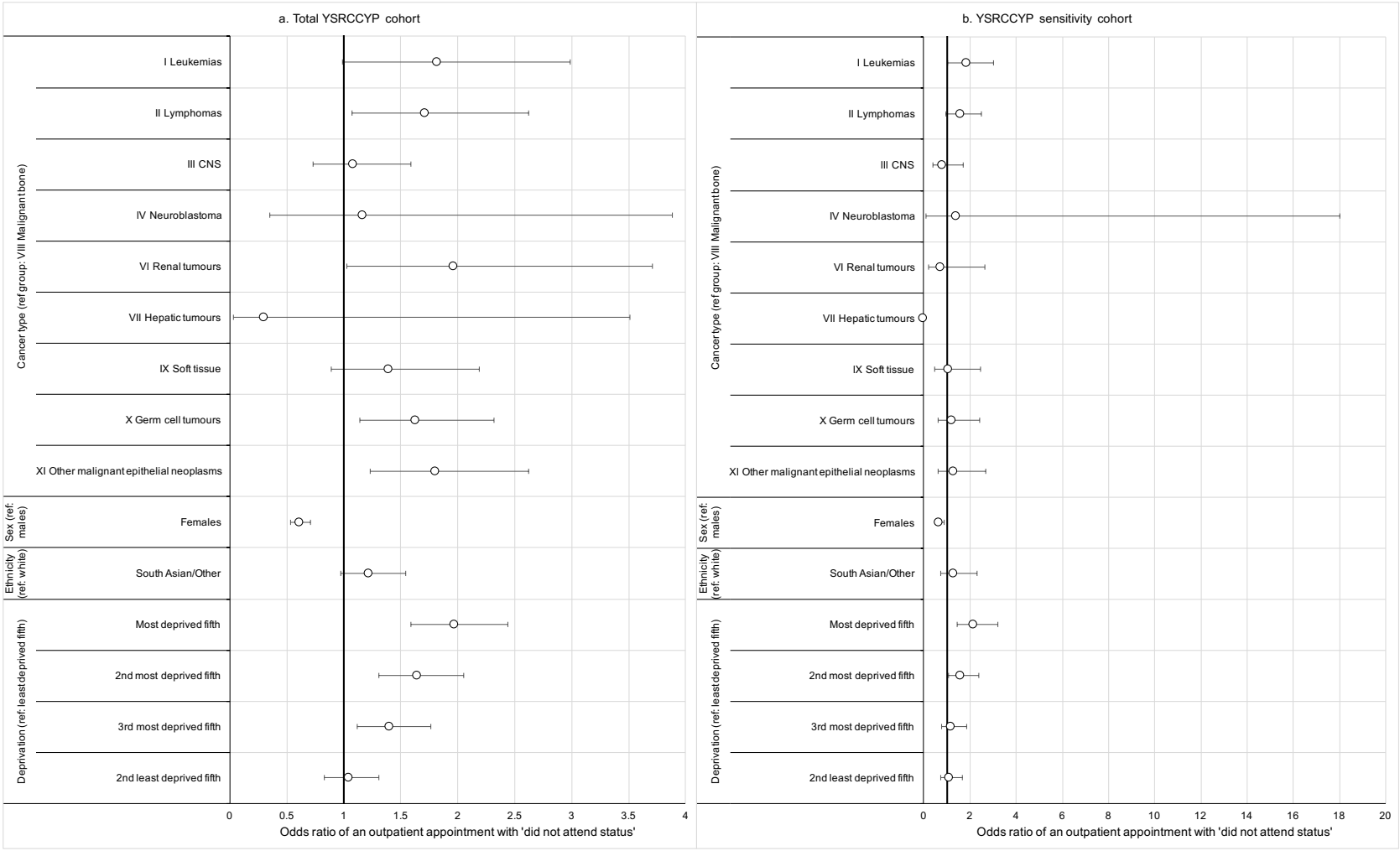


Figure 6.15: Odds ratios of 'did not attend' (DNA) status from mixed effects logistic regression model with 95% confidence intervals by cancer type – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.3.6 Outpatient appointments by treatment specialty.

The odds of an outpatient appointment with a DNA status was highest for the mental health treatment specialty and was significantly higher than the oncology treatment speciality in both early (1.45; 95% CI 1.1 to 1.9) (Figure 6.16) and late cancer onset (2.23; 95% CI 1.75 to 2.85) (Figure 6.17). Only maternity/obstetrics/gynaecology had significantly lower odds of a DNA appointment compared with oncology in both early (0.65; 95% CI 0.55 to 0.76) and late cancer onset (0.52; 95% CI 0.46 to 0.6).

The odds ratios in the sensitivity cohort for mental health and maternity/obstetrics/gynaecology were similar to all sensitivity cohorts. There were some differences for other treatment specialties where the odds of a DNA appointment were found to be significantly different compared with oncology in the YSRCCYP cohort but not in the sensitivity cohort, and vice versa. Despite these differences, there were no significant differences in odds between the models.

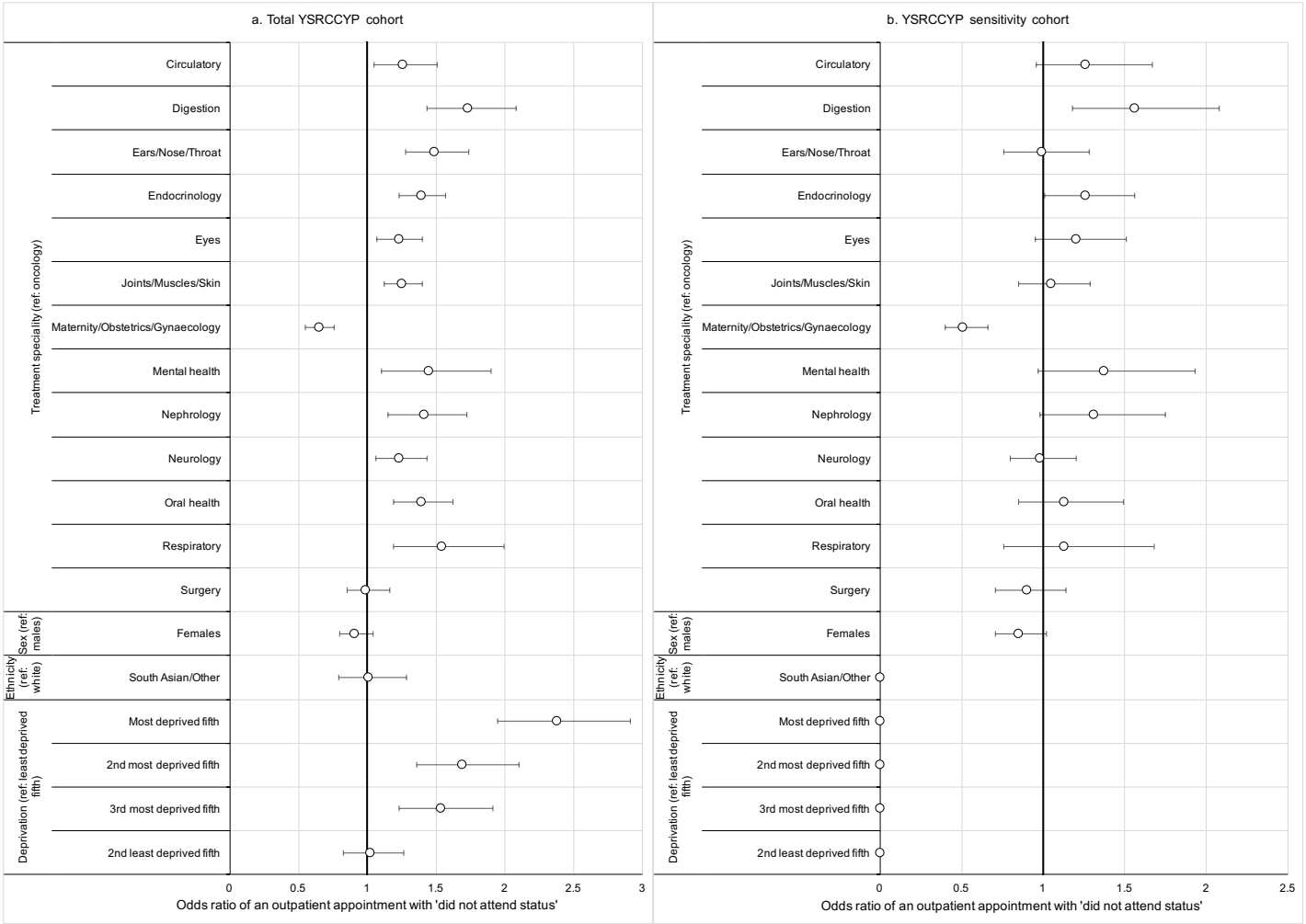


Figure 6.16: Odds ratios of 'did not attend' (DNA) status from mixed effects logistic regression model with 95% confidence intervals by treatment specialty – early cancer onset (a.) and equivalent sensitivity cohort (b.).

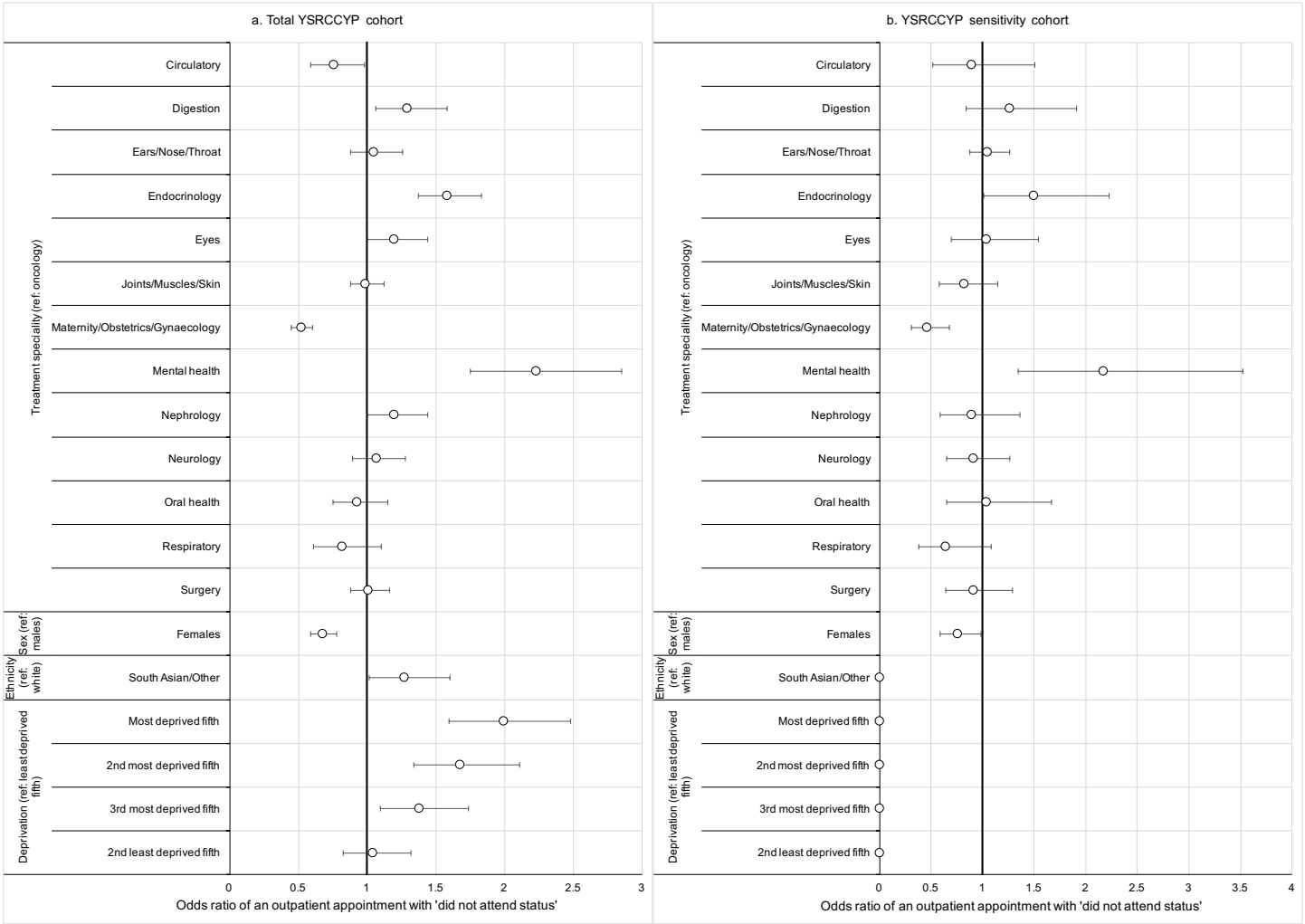


Figure 6.17: Odds ratios of 'did not attend' (DNA) status from mixed effects logistic regression model with 95% confidence intervals by treatment specialty – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.3.7 Outpatient appointment attendance status by mental health admission.

The YSRCCYP cohort was linked to both the mental health and outpatient HES data to determine whether having a previous mental health admission was associate with outpatient appointment status.

Of the 4,735 individuals with an outpatient appointment, 490 (10.3%) had a mental health admission before any outpatient appointment. There was a higher percentage of individuals with a mental health admission in the late cancer onset group (n=288; 11.9% of the late cancer onset total) compared with early cancer onset (n=202; 8.7% of the early cancer onset total).

By deprivation group, there were twice the number of individuals with a mental health admission in the most deprived group (n=150; 13.1% of the most deprived fifth total) compared with the least deprived fifth (n=63; 7.7% of the least deprived fifth total) (Table 6.6).

Table 6.6: Number of individuals with a mental health admission any time before an outpatient appointment by socio-demographic groups.

		Total individuals with a mental health admission before an outpatient appointment			Total individuals with an outpatient appointment
		N	% of group	% of total	
Age at cancer diagnosis	0 to 14 years (early onset)	202	8.7	4.3	2,313
	15 to 29 years (late onset)	288	11.9	6.1	2,422
Sex	Males	273	9.8	5.8	2,780
	Females	217	11.1	4.6	1,955
Ethnicity	White	378	10.1	8.0	3,740
	South Asian/Other	36	9.1	0.8	394
Deprivation	Least deprived fifth	63	7.7	1.3	823
	2nd least deprived fifth	86	9.3	1.8	927
	3rd most deprived fifth	84	10.1	1.8	829
	2nd most deprived fifth	90	11.0	1.9	815
	Most deprived fifth	150	13.1	3.2	1,142
Total		490	10.3	10.3	4,735

Individuals diagnosed with soft tissue tumours had the highest percentage of individuals with a mental health admission before an outpatient appointment at 13.9% (n=35), followed by CNS neoplasms (n=98; 13.4%) and other malignant epithelial neoplasms (n=38; 11.4%) (Table 6.7).

Table 6.7: Number of individuals with a mental health admission any time before an outpatient appointment by cancer type.

	Total individuals with a mental health admission before an outpatient appointment			Total individuals with an outpatient appointment
	N	% of group	% of total	
I Leukaemias	80	8.4	1.7	956
II Lymphomas	107	10.4	2.3	1,028
III CNS	98	13.4	2.1	732
IV Neuroblastoma	10	9.0	0.2	111
V Retinoblastoma	7	7.0	0.1	100
VI Renal tumours	14	7.3	0.3	193
VIII Malignant bone	18	10.2	0.4	177
IX Soft tissue	35	13.9	0.7	251
X Germ cell tumours	82	10.0	1.7	823
XI Other malignant epithelial neoplasms	38	11.4	0.8	334
Total	490	10.3	10.3	4,735

Of the 122,422 outpatient appointments for the YSRCCYP cohort, 13,450 (11%) occurred after a mental health admission. Of these 13,450 outpatient appointments, 1,891 (14%) had a DNA status (Figure 6.18). This was higher than the percentage in the overall YSRCCYP cohort with an outpatient appointment of 10.3%.

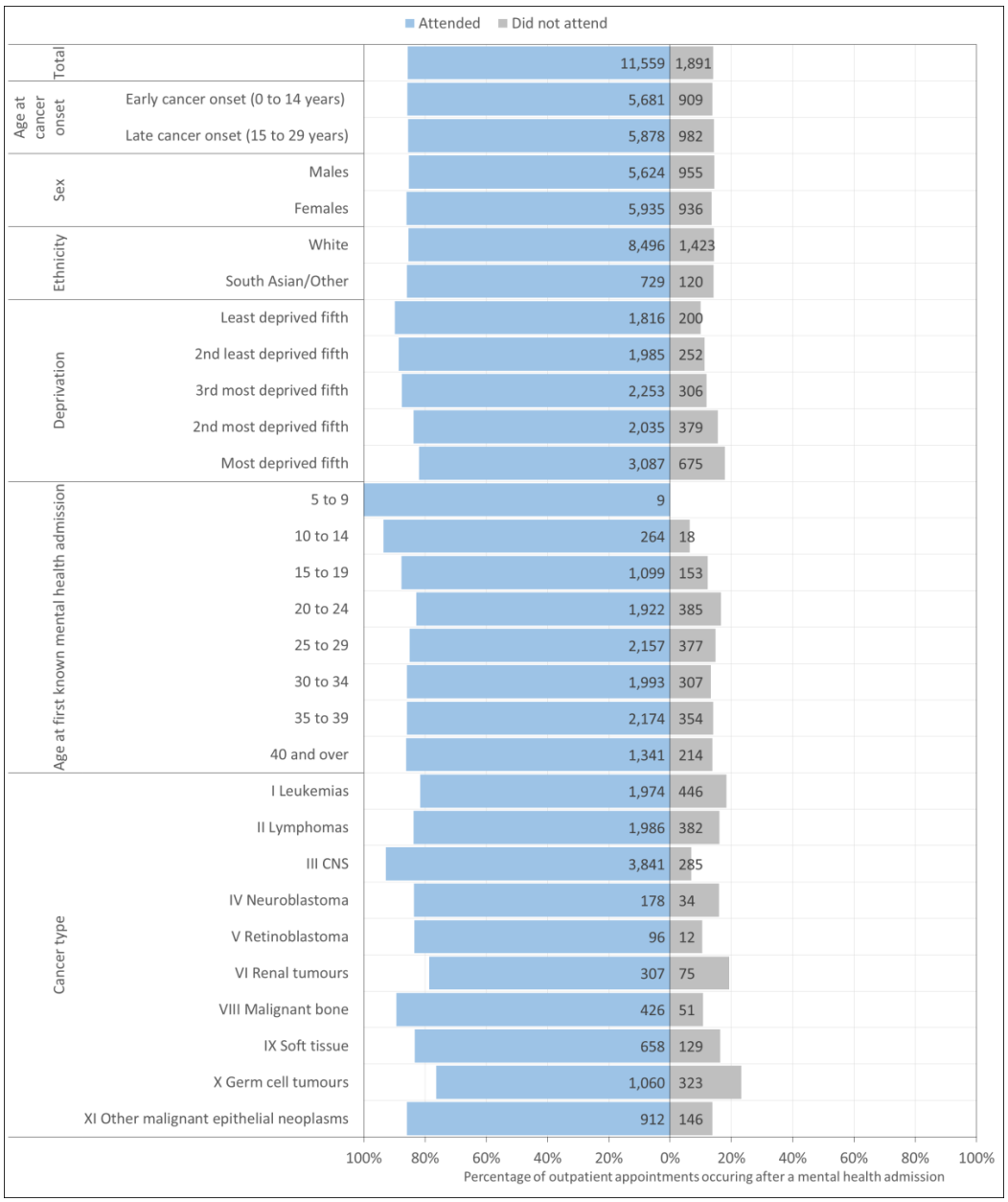


Figure 6.18: Percentage (and number) of outpatient appointments occurring after a mental health admission by attendance status.

Multi-level logistic regression modelling for the overall cohort found that the odds of not attending an outpatient appointment with a previous mental health admission was significantly higher than for individuals with no previous mental health admission by 60% (Figure 6.19).

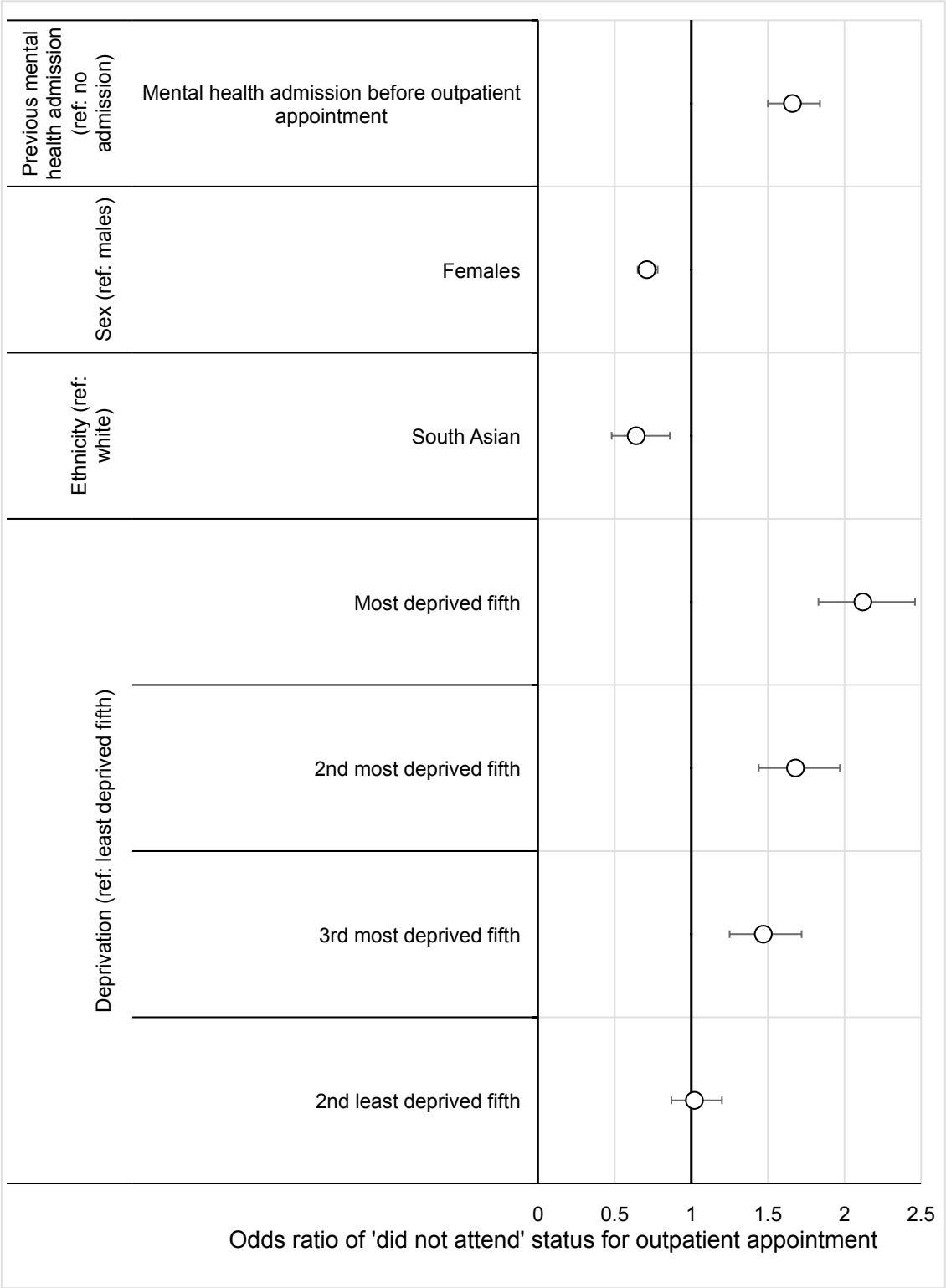


Figure 6.19: Odds ratios of 'did not attend' (DNA) status from mixed effects logistic regression model with 95% confidence intervals by previous mental health admission.

6.3.4 Inpatient admission data analysis.

6.3.4.1 Demographics.

There were 3,666 individuals (62.8% of eligible individuals) matched on the inpatient dataset. The percentage of individuals with an inpatient admission by age at cancer onset group, sex and deprivation of the matched cohort were similar to the percentages in the overall YSRCCYP cohort and had a slightly higher percentage of individuals with white ethnicity at 77.4% (Figure 6.20), compared with 68.9% in the overall YSRCCYP cohort (Figure 6.1).

By cancer type, the highest number of individuals with an inpatient admission were diagnosed with lymphomas (n=747; 20.4%), leukaemias (n=713; 19.4%) and CNS neoplasms (n=682; 18.6%). The cancer type with the lowest number of individuals with an inpatient admission were hepatic tumours (n=20; 0.5%), retinoblastomas (n=70; 1.9%) and neuroblastomas (n=80; 2.2%) (Figure 6.20).

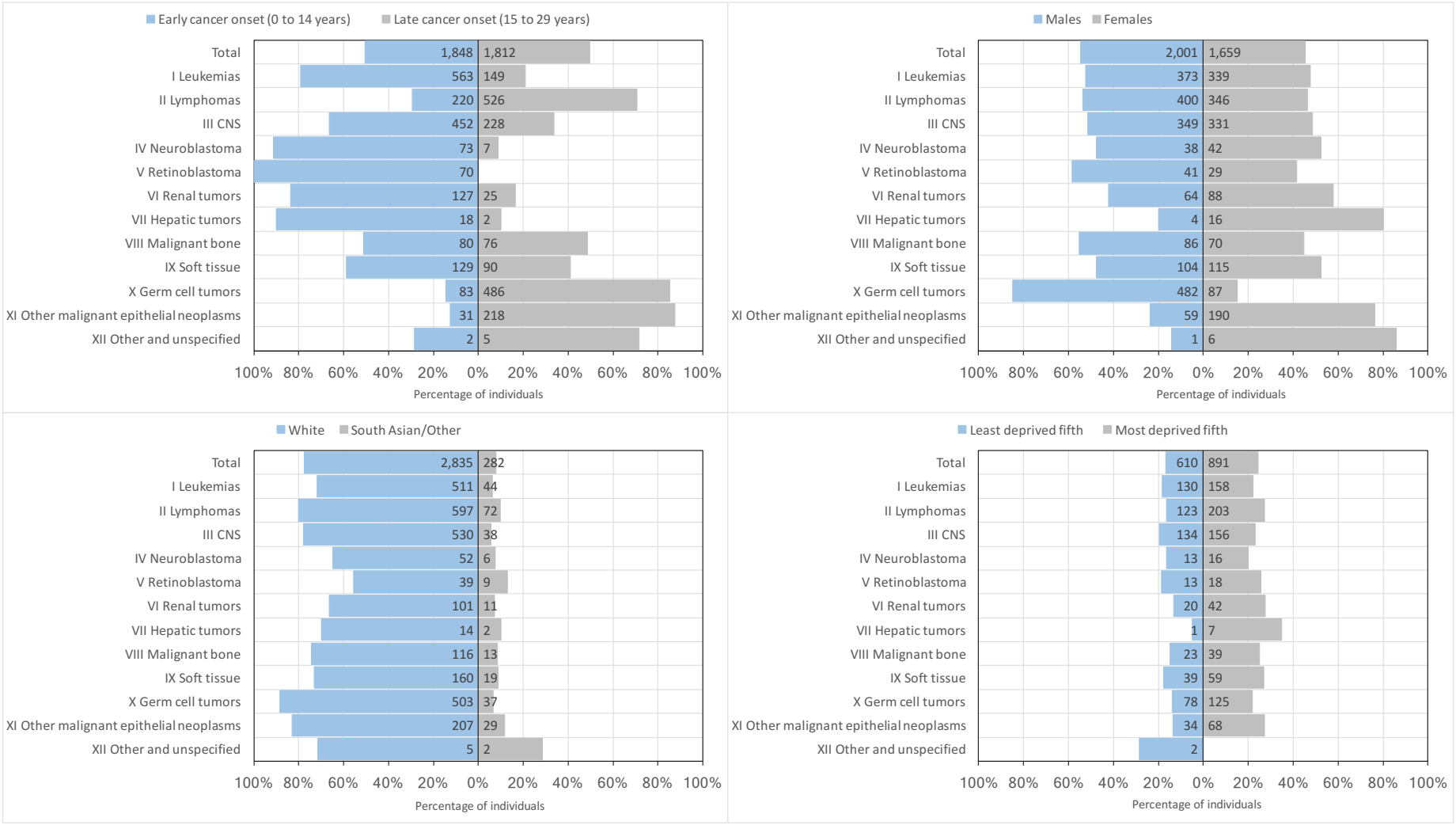


Figure 6.20: Percentage (and number) of individuals linked to inpatient data by cancer type and socio-demographic groups.

6.3.4.2 Total continuous inpatient spells (CIPS) by socio-demographic groups, cancer type, diagnosis type and treatment specialty.

There were 26,203 CIPS. The mean number of CIPS for an individual was 7.2 (range 1 to 171). The mean number of CIPS was higher by around 2 in early cancer onset compared with late cancer onset. Females had a higher mean CIPS per individuals by 1 compared with males. Mean CIPS per individuals by ethnicity and deprivation categories were similar to the overall mean. The most deprived fifth had the highest total of CIPS (n=6,653; 25.4%), although the mean number of admissions individual was similar to the least deprived fifth. The third most deprived fifth had the smallest total of CIPS (n=3,895; 14.9%) and the smallest mean admission per individual at 5.9 (range 1 to 72) (Table 6.8).

The total number of CIPS was slightly higher during the transitional care period (n=11,043; 42.1%) compared with after the transitional care period (n=10,759; 41.1%). Before the transitional care period, there was a total of 4,401 CIPS (16.8%). By 5-year age bands, the total of CIPS increased for each category up to the 25 to 29-year age group, before decreasing. The age group with the highest mean CIPS per individual was the 10 to 15-year group at 4.9 (range 1 to 136) (Table 6.8).

Table 6.8: Descriptive statistics of continuous inpatient spells (CIPS) by socio-demographic groups.

		Total continuous inpatient spells (CIPS)				
		N	**% of total CIPS**	**Mean**	**Median (range)**	**Standard deviation**
Age at cancer diagnosis	0 to 14 years (early onset)	14,973	57.1	8.1	3 (1 to 152)	14.0
	15 to 29 years (late onset)	11,230	42.9	6.2	3 (1 to 171)	11.9
Sex	Males	13,171	50.3	6.6	2 (1 to 171)	13.7
	Females	13,032	49.7	7.9	4 (1 to 152)	12.2
Ethnicity	White	19,847	75.7	7.0	3 (1 to 171)	13.3
	South Asian/Other	1,951	7.4	6.9	3 (1 to 158)	13.7
Deprivation	Least deprived fifth	4,623	17.6	7.6	3 (1 to 171)	14.7
	2nd least deprived fifth	4,987	19.0	7.1	3 (1 to 124)	13.2
	3rd most deprived fifth	3,895	14.9	5.9	3 (1 to 72)	9.1

	2nd most deprived fifth	4,860	18.5	7.4	3 (1 to 158)	14.1
	Most deprived fifth	6,653	25.4	7.5	3 (1 to 119)	11.9
Age at inpatient admission	5 to 9	1,678	6.4	4.7	2 (1 to 86)	9.7
	10 to 14	2,723	10.4	4.9	2 (1 to 136)	11.6
	15 to 19	3,336	12.7	4.4	2 (1 to 86)	8.6
	20 to 24	3,506	13.4	4.0	2 (1 to 145)	7.8
	25 to 29	4,201	16.0	4.0	2 (1 to 156)	8.5
	30 to 34	4,147	15.8	3.5	2 (1 to 122)	6.1
	35 to 39	3,609	13.8	3.7	2 (1 to 124)	7.2
	40 and over	3,003	11.5	4.3	2 (1 to 79)	6.7
Total		26,203	100.0	7.2	3 (1 to 171)	13.0

Individuals diagnosed with leukaemia (n=6,008; 22.9%), lymphomas (n=5,502; 21%) and CNS neoplasms (n=5,251; 20%) had the highest total of CIPS. The cancer types with the highest mean CIPS per individual were malignant bone tumours (8.8 CIPS per individual; range 1 to 116), renal tumours (8.5 CIPS per individual; range 1 to 145) and leukaemias (8.4 CIPS per individual; range 1 to 152). The cancer types with the lowest mean inpatient admissions per individual were germ cell tumours (4 CIPS per individual; range 1 to 51), hepatic tumours (4.4 CIPS per individual; range 1 to 14) and retinoblastoma (5.2 CIPS per individual; range 1 to 43) (Table 6.9).

Table 6.9: Descriptive statistics of continuous inpatient spells (CIPS) by cancer type.

	Total inpatient admissions				
	N	**% of total admissions**	**Mean**	**Median (range)**	**Standard deviation**
I Leukaemias	6,008	22.9	8.4	3 (1 to 152)	15.2
II Lymphomas	5,502	21.0	7.4	3 (1 to 171)	15.0
III CNS	5,251	20.0	7.7	4 (1 to 156)	11.8
IV Neuroblastoma	518	2.0	6.5	3 (1 to 65)	9.9
V Retinoblastoma	366	1.4	5.2	3 (1 to 43)	8.0
VI Renal tumours	1,295	4.9	8.5	3 (1 to 145)	17.7
VII Hepatic tumours	88	0.3	4.4	3.5 (1 to 14)	3.7
VIII Malignant bone	1,371	5.2	8.8	4 (1 to 116)	13.8
IX Soft tissue	1,759	6.7	8.0	3 (1 to 119)	13.6
X Germ cell tumours	2,275	8.7	4.0	2 (1 to 51)	5.9
XI Other malignant epithelial	1,721	6.6	6.9	3 (1 to 124)	12.4

neoplasms					
Total	26,244	100.0	7.2	3 (1 to 171)	13.0

Over 30% of all CIPS had a primary diagnosis of neoplasm (n=8,305; 31.7%) (Table 6.10). For all cancer types, neoplasms was one of the top three highest totals of CIPS by primary diagnosis with a percentage ranging between 14.5% (n=186) for renal tumours to 38.4% (n=139) for retinoblastomas (Figure 6.11). Injury, poisoning and certain other consequences of external causes had the second highest total of CIPS (n=2,452; 9.4%) and was one of the top three highest total of CIPS for eight cancer types (leukaemia, CNS neoplasms, neuroblastomas, renal tumours, hepatic tumours, soft cell tumours, germ cell tumours and other epithelial tumours) (Figure 6.11). Congenital malformations (n=3; 0.01%), diseases of the ear (n=164; 0.6%) and mental and behavioural problems (n=202; 0.8%) had the lowest number of CIPS by primary diagnosis.

Table 6.10: Descriptive statistics of continuous inpatient spells (CIPS) by primary diagnosis.

	Total inpatient admissions				
	N	**% of total admissions**	**Mean**	**Median (range)**	**Standard deviation**
Certain infectious and parasitic diseases	434	1.7	7.0	3 (1 to 51)	10.2
Neoplasms	8,305	31.7	15.1	7 (1 to 156)	20.4
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	512	2.0	14.2	7.5 (1 to 152)	28.6
Endocrine, nutritional and metabolic diseases	966	3.7	9.2	4.5 (1 to 122)	15.3
Mental and behavioural disorders	202	0.8	6.8	3 (1 to 44)	10.1
Diseases of the nervous system	740	2.8	8.6	5 (1 to 96)	12.4
Diseases of the eye and adnexa	366	1.4	4.7	2 (1 to 33)	6.1
Diseases of the ear and mastoid process	164	0.6	3.3	2 (1 to 17)	3.4
Diseases of the circulatory system	563	2.1	6.6	3 (1 to 171)	9.6
Diseases of the respiratory system	792	3.0	7.8	3 (1 to 171)	18.1
Diseases of the digestive system	2,066	7.9	4.2	2 (1 to 100)	6.8
Diseases of the skin and subcutaneous tissue	482	1.8	4.2	2 (1 to 116)	11.4
Diseases of the musculoskeletal system and connective tissue	1,055	4.0	5.7	2 (1 to 105)	11.5
Diseases of the	1,233	4.7	6.2	3 (1 to 158)	12.9

genitourinary system					
Pregnancy, childbirth and the puerperium/Certain conditions originating in the perinatal period	1,836	7.0	5.4	4 (1 to 54)	5.9
Congenital malformations, deformations and chromosomal abnormalities	3	0.01	-	3 (3 to 3)	-
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	188	0.7	3.3	3 (1 to 13)	2.7
Injury, poisoning and certain other consequences of external causes	2,452	9.4	6.2	(1 to 143)	11.8
Factors influencing health status and contact with health services	1,630	6.2	4.8	2 (1 to 81)	7.5
Total	26,203	100.0	7.2	3 (1 to 171)	13.0

As with outpatient appointments, oncology had the highest total of CIPS by treatment specialty (n=5,804; 22.2%), followed by maternity/obstetrics/gynaecology (n=2,224; 8.5 5) and surgery (n=2,086; 8%). Mental health had the lowest number of CIPS by treatment specialty (n=99; 0.4%). There were no mental health CIPS for individuals diagnosed with neuroblastoma, hepatic tumours and soft tissue tumours (Figure 6.12).

Table 6.11: Number of continuous inpatient spells (CIPS) by cancer type and primary diagnosis.

	I Leukaemias		II Lymphomas		III CNS		IV Neuroblastoma		V Retinoblastoma	
	N	%	N	%	N	%	N	%	N	%
Certain infectious and parasitic diseases	124	2.1	107	2.0	64	1.2	9	1.8	5	1.4
Neoplasms	**2,246**	**37.8**	**1,888**	**34.6**	**1,669**	**32.3**	**106**	**20.8**	**139**	**38.4**
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	123	2.1	219	4.0	61	1.2	16	3.1	6	1.7
Endocrine, nutritional and metabolic diseases	310	5.2	74	1.4	250	4.8	28	5.5	-	-
Mental and behavioural disorders	13	0.2	39	0.7	66	1.3	3	0.6	3	0.8
Diseases of the nervous system	83	1.4	37	0.7	**444**	**8.6**	28	5.5	1	0.3
Diseases of the eye and adnexa	81	1.4	29	0.5	89	1.7	5	1.0	**35**	**9.7**
Diseases of the ear and mastoid process	44	0.7	15	0.3	38	0.7	7	1.4	7	1.9
Diseases of the circulatory system	152	2.6	121	2.2	56	1.1	7	1.4	1	0.3
Diseases of the respiratory system	140	2.4	222	4.1	113	2.2	31	6.1	11	3.0
Diseases of the digestive system	397	6.7	**496**	**9.1**	303	5.9	35	6.9	20	5.5
Diseases of the skin and subcutaneous tissue	92	1.5	114	2.1	72	1.4	9	1.8	9	2.5
Diseases of the musculoskeletal system and connective tissue	189	3.2	221	4.0	192	3.7	25	4.9	3	0.8
Diseases of the genitourinary system	207	3.5	334	6.1	135	2.6	33	6.5	9	2.5
Pregnancy, childbirth and the puerperium/Certain conditions originating in the perinatal period	379	6.4	**511**	**9.4**	213	4.1	**53**	**10.4**	19	5.2
Congenital malformations, deformations and chromosomal abnormalities	-	-	1	-	1	-	-	-	-	-

Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	26	0.4	10	0.2	92	1.8	8	1.6	2	0.6
Injury, poisoning and certain other consequences of external causes	**431**	**7.3**	483	8.8	**596**	**11.5**	**41**	**8.0**	24	6.6
Factors influencing health status and contact with health services	**416**	**7.0**	254	4.7	241	4.7	21	4.1	**26**	**7.2**
Total	5,939	100.0	5,460	100.0	5,163	100.0	510	100.0	362	100.0

Figures in **bold** represent the 3 primary diagnoses with the highest total of CIPS within the cancer type category.

Table 6.11 continued: Number of continuous inpatient spells (CIPS) by cancer type and primary diagnosis.

	VI Renal tumours		**VII Hepatic tumours**		**VIII Malignant bone**		**IX Soft tissue**		**X Germ cell tumours**		**XI Other malignant epithelial neoplasms**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Certain infectious and parasitic diseases	32	2.5	8	9.1	16	1.2	20	1.1	24	1.1	15	0.9
Neoplasms	**186**	**14.5**	**13**	**14.8**	**471**	**35.1**	**562**	**32.2**	**422**	**18.8**	**494**	**28.8**
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	20	1.6	-	-	5	0.4	23	1.3	11	0.5	22	1.3
Endocrine, nutritional and metabolic diseases	128	10.0	4	4.5	11	0.8	51	2.9	75	3.3	35	2.0
Mental and behavioural disorders	4	0.3	-	-	3	0.2	5	0.3	46	2.1	8	0.5
Diseases of the nervous system	6	0.5	-	-	10	0.7	13	0.7	56	2.5	37	2.2
Diseases of the eye and adnexa	18	1.4	-	-	23	1.7	17	1.0	46	2.1	22	1.3

Diseases of the ear and mastoid process	10	0.8	3	3.4	2	0.1	18	1.0	9	0.4	7	0.4
Diseases of the circulatory system	27	2.1	-	0.0	23	1.7	63	3.6	69	3.1	18	1.0
Diseases of the respiratory system	56	4.4	2	2.3	23	1.7	56	3.2	75	3.3	41	2.4
Diseases of the digestive system	99	7.7	4	4.5	69	5.1	**132**	**7.6**	**286**	**12.8**	**207**	**12.1**
Diseases of the skin and subcutaneous tissue	32	2.5	-	-	25	1.9	38	2.2	59	2.6	29	1.7
Diseases of the musculoskeletal system and connective tissue	33	2.6	2	2.3	65	4.9	66	3.8	143	6.4	111	6.5
Diseases of the genitourinary system	75	5.8	5	5.7	45	3.4	115	6.6	154	6.9	111	6.5
Pregnancy, childbirth and the puerperium/Certain conditions originating in the perinatal period	**141**	**11.0**	**14**	**15.9**	**93**	**6.9**	126	7.2	128	5.7	151	8.8
Congenital malformations, deformations and chromosomal abnormalities	-	-	-	-	-	-	1	0.1	-	-	-	-
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	24	1.9	-	-	1	0.1	11	0.6	10	0.4	2	0.1
Injury, poisoning and certain other consequences of external causes	**148**	**11.5**	**12**	**13.6**	79	5.9	**161**	**9.2**	**284**	**12.7**	**156**	**9.1**
Factors influencing health status and contact with health services	55	4.3	3	3.4	**211**	**15.7**	107	6.1	189	8.4	58	3.4
Total	1,283	100.0	88	100.0	1,340	100.0	1,744	100.0	2,240	100.0	1,715	100.0

Figures in **bold** represent the 3 primary diagnoses with the highest total of CIPS within the cancer type category.

Table 6.12: Number of continuous inpatient spells (CIPS) by cancer type and treatment specialty.

	I Leukaemias		II Lymphomas		III CNS		IV Neuroblastoma		V Retinoblastoma	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Circulatory	92	1.5	99	1.8	16	0.3	2	0.4	5	1.4
Digestion	201	3.4	182	3.3	86	1.7	6	1.2	5	1.4
Ears/Nose/ Throat	108	1.8	105	1.9	61	1.2	12	2.4	8	2.2
Endocrinology	90	1.5	23	0.4	215	4.2	8	1.6	1	0.3
Eyes	69	1.2	25	0.5	69	1.3	1	0.2	**82**	**22.7**
Joints/Muscles/Skin	168	2.8	173	3.2	145	2.8	**31**	**6.1**	**30**	**8.3**
Maternity/Obstetrics/ Gynaecology	**440**	**7.4**	**630**	**11.5**	244	4.7	**62**	**12.2**	20	5.5
Mental health	8	0.1	13	0.2	23	0.4	-	-	3	0.8
Nephrology	122	2.1	265	4.9	77	1.5	21	4.1	4	1.1
Neurology	63	1.1	26	0.5	**765**	**14.8**	16	3.1	1	0.3
Oncology	**1,775**	**29.9**	**1,739**	**31.9**	**881**	**17.1**	25	4.9	**38**	**10.5**
Oral health	100	1.7	104	1.9	115	2.2	9	1.8	13	3.6
Respiratory	21	0.4	63	1.2	30	0.6	10	2.0	2	0.6
Surgery	**346**	**5.8**	**480**	**8.8**	**289**	**5.6**	**41**	**8.0**	24	6.6
Total	5,937	100.0	5,458	100.0	5,161	100.0	510	100.0	362	100.0

Figures in **bold** represent the 3 treatment specialties with the highest total of CIPS within the cancer type category.

Table 6.12 continued: Number of continuous inpatient spells (CIPS) by cancer type and treatment specialty.

	VI Renal tumours		VII Hepatic tumours		VIII Malignant bone		IX Soft tissue		X Germ cell tumours		XI Other malignant epithelial neoplasms	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Circulatory	9	0.7	-	-	22	1.6	60	3.4	25	1.1	15	0.9
Digestion	**151**	**11.8**	**13**	**14.8**	18	1.3	44	2.5	123	5.5	103	6.0
Ears/Nose/ Throat	24	1.9	3	3.4	12	0.9	31	1.8	37	1.7	40	2.3
Endocrinology	3	0.2	-	-	9	0.7	9	0.5	38	1.7	101	5.9
Eyes	23	1.8	-	-	9	0.7	15	0.9	33	1.5	19	1.1
Joints/Muscles /Skin	30	2.3	1	1.1	**279**	**20.8**	72	4.1	136	6.1	58	3.4
Maternity/ Obstetrics/ Gynaecology	**180**	**14.0**	**12**	**13.6**	**113**	**8.4**	**161**	**9.2**	151	6.8	**198**	**11.6**
Mental health	2	0.2	-	-	1	0.1	-	-	33	1.5	3	0.2
Nephrology	92	7.2	-	-	24	1.8	49	2.8	**187**	**8.4**	50	2.9
Neurology	5	0.4	-	-	9	0.7	9	0.5	57	2.5	11	0.6
Oncology	129	10.1	**10**	**11.4**	**288**	**21.5**	**309**	**17.7**	**238**	**10.6**	**318**	**18.6**
Oral health	22	1.7	-	-	14	1.0	35	2.0	52	2.3	38	2.2
Respiratory	4	0.3	1	1.1	10	0.7	20	1.1	14	0.6	8	0.5
Surgery	**134**	**10.5**	8	9.1	77	5.8	**197**	**11.3**	**277**	**12.4**	**191**	**11.1**
Total	1,282	100.0	88	100.0	1,339	100.0	1,743	100.0	2,237	100.0	1,714	100.0

Figures in **bold** represent the 3 treatment specialties with the highest total of CIPS within the cancer type category.

6.3.4.3 Incidence rates for continuous inpatient spells (CIPS).

The overall incidence rate for CIPS was 390.4 per 1,000 person-years (95% CI 385.7 to 395.1 per 1,000 person-years), 389.9 per 1,000 person-years (95% CI 383.7 to 396.82 per 1,000 person-years) in early cancer onset (Figure 6.21) and 391 per 1,000 person-years (95% CI 383.8 to 398.3 per 1,000 person-years) in late cancer onset (Figure 6.22).

In early cancer onset, the incidence rate of CIPS for females was around 30% higher than males at 445 per 1,000 person-years (95% CI 435.2 to 455.1 per 1,000 person-years) (Figure 6.21). In late cancer onset, the incidence rate for females was around 69% higher compared with males at 520.4 per 1,000 person-years (95% CI 506.7 to 534.6 per 1,000 person-years) and was significantly higher compared with early cancer onset (Figure 6.22).

South Asian/Other ethnicity had a lower incidence rate for CIPS compared with white ethnicity in early cancer onset (unknown ethnicity in early cancer onset had an incidence rate of 231 per 1,000 person-years (95% CI 224.2 to 238 per 1,000 person-years)) and had a higher incidence rate in late cancer onset. However, these differences were not statistically significant.

Analysis by deprivation groups showed the two most deprived fifths had a higher CIPS incidence rate compared with the three least deprived fifths in both early and late cancer onset. The lowest CIPS incidence rate was found in the third most deprived fifth in early cancer onset and in the second least deprived fifth in late cancer onset.

During the transitional care period, the incidence rate decreased in the 20 to 24-year age group, which had the lowest incidence rate in early cancer onset (332.6 per 1,000 person-year; 95% CI 319.9 to 345.8 per 1,000 person-years). This contrasted with late cancer onset where the 20 to 24-year age group had the highest incidence rate of 635.6 per 1,000 person-year (95% CI 596.8 to 676.8 per 1,000 person-years).

For lymphomas (261 per 1,000 person-year; 95% CI 248.1 to 274.5 per 1,000 person-year) and neuroblastomas (275.4 per 1,000 person-year; 95% CI 251.1 to 301.9 per 1,000 person-year), there was a significantly lower incidence rate compared with the total incidence in early cancer onset. However, in late cancer onset, these cancer types were significantly higher than the total incidence rate.

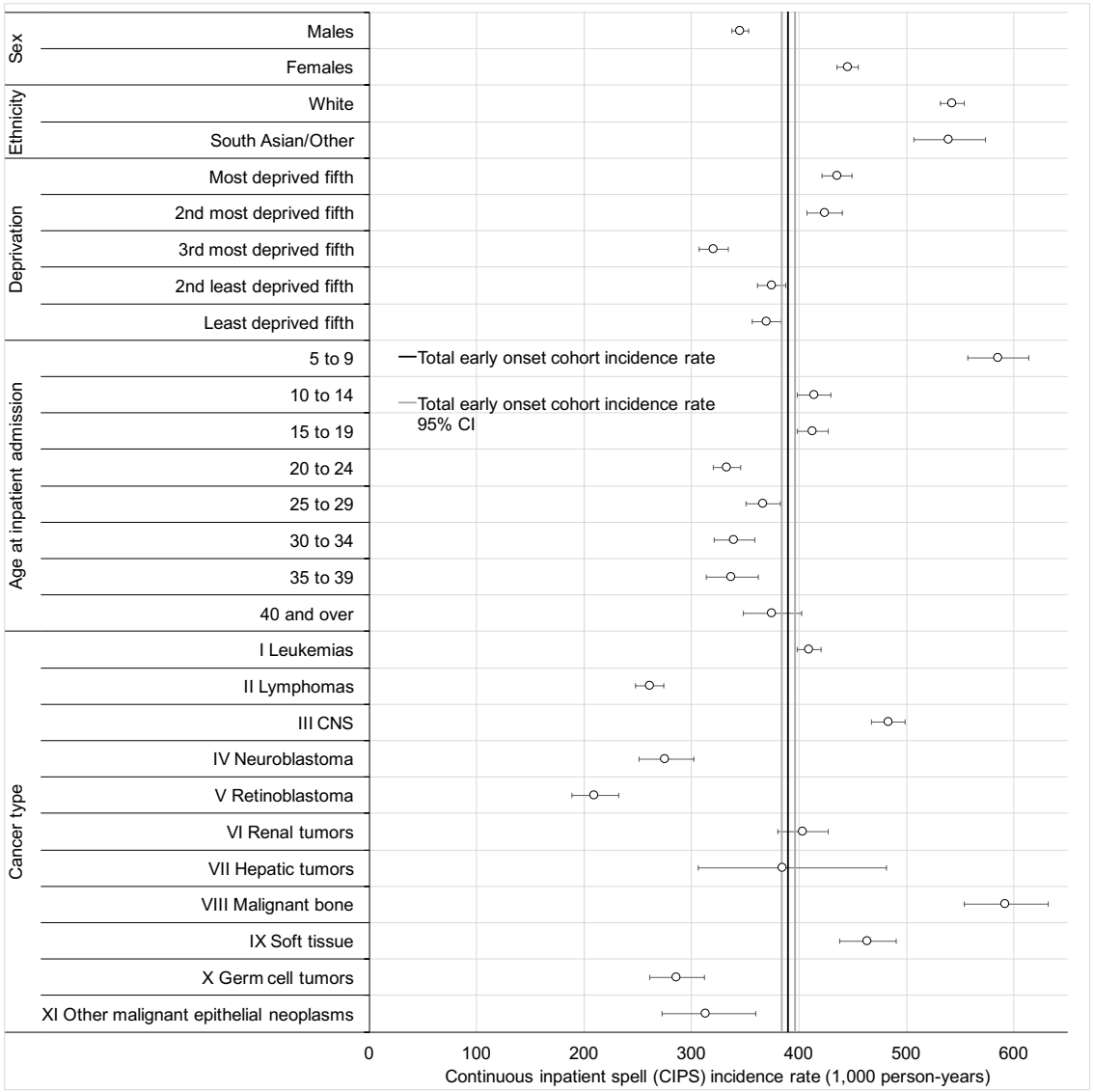


Figure 6.21: Incidence rate per 1,000 person-years for continuous inpatient spell (CIPS) - early cancer onset.

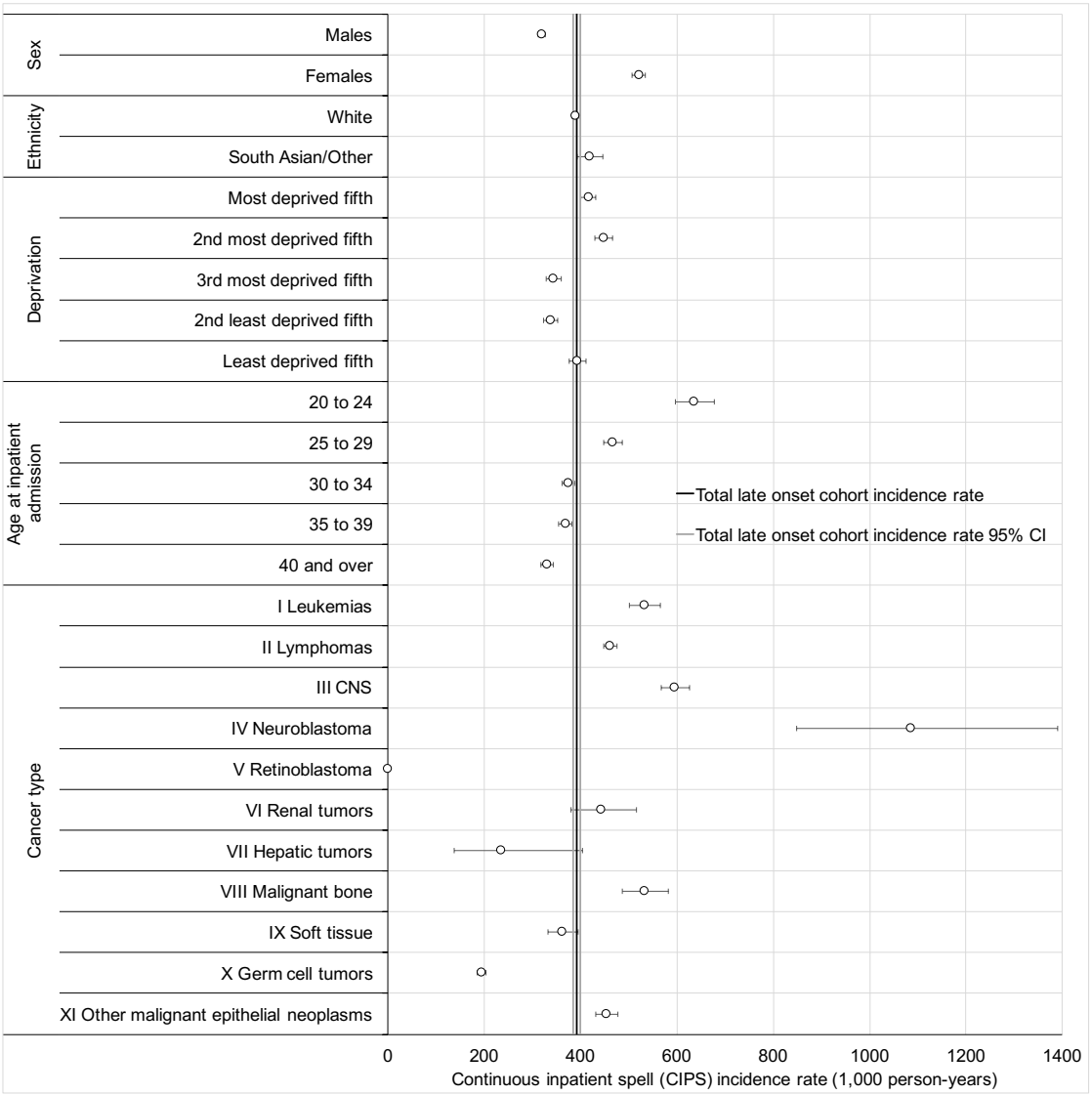


Figure 6.22: Incidence rate per 1,000 person-years for continuous inpatient spell (CIPS) - late cancer onset.

6.3.4.4 Inpatient admission by age at inpatient admission.

The older age groups during and after the transitional care period in early onset had significantly higher risk of a CIPS compared with the 10 to 14-year age group, with the risk increasing by about 20% to 30% by each 5-year age group up to the 35 to 39 group, with a relative risk of 2.33 (95%CI 2.11 to 2.55). The relative risk then increased by two-fold for the 40 and over age group at 4.93 (95%CI 4.45 to 5.47). However, in the sensitivity cohort in early cancer onset, the trend was opposite, where each increase in age category had a decreased risk of a CIPS (Figure 6.23).

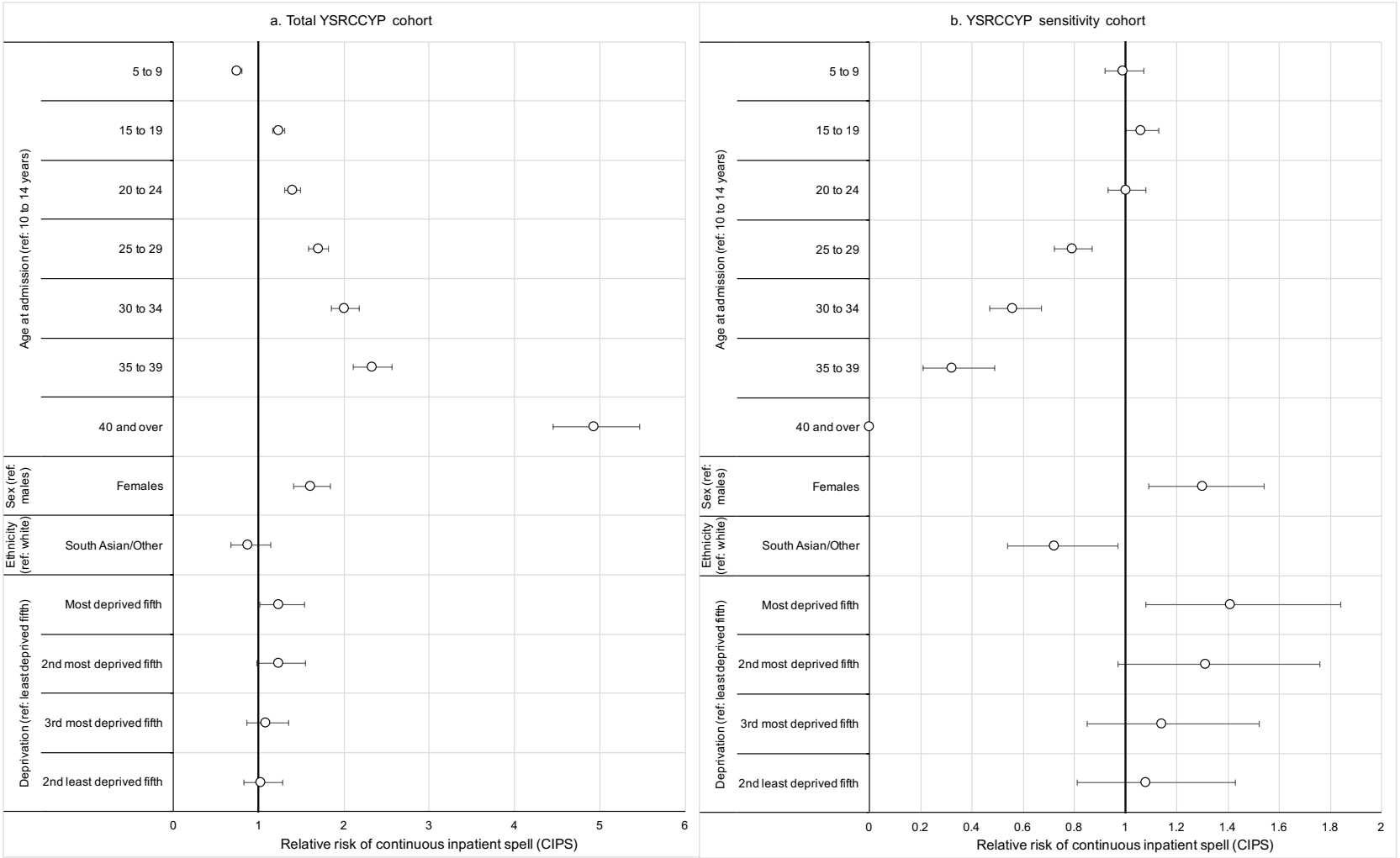


Figure 6.23: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals by age at CIPS – early cancer onset (a.) and equivalent sensitivity cohort (b.).

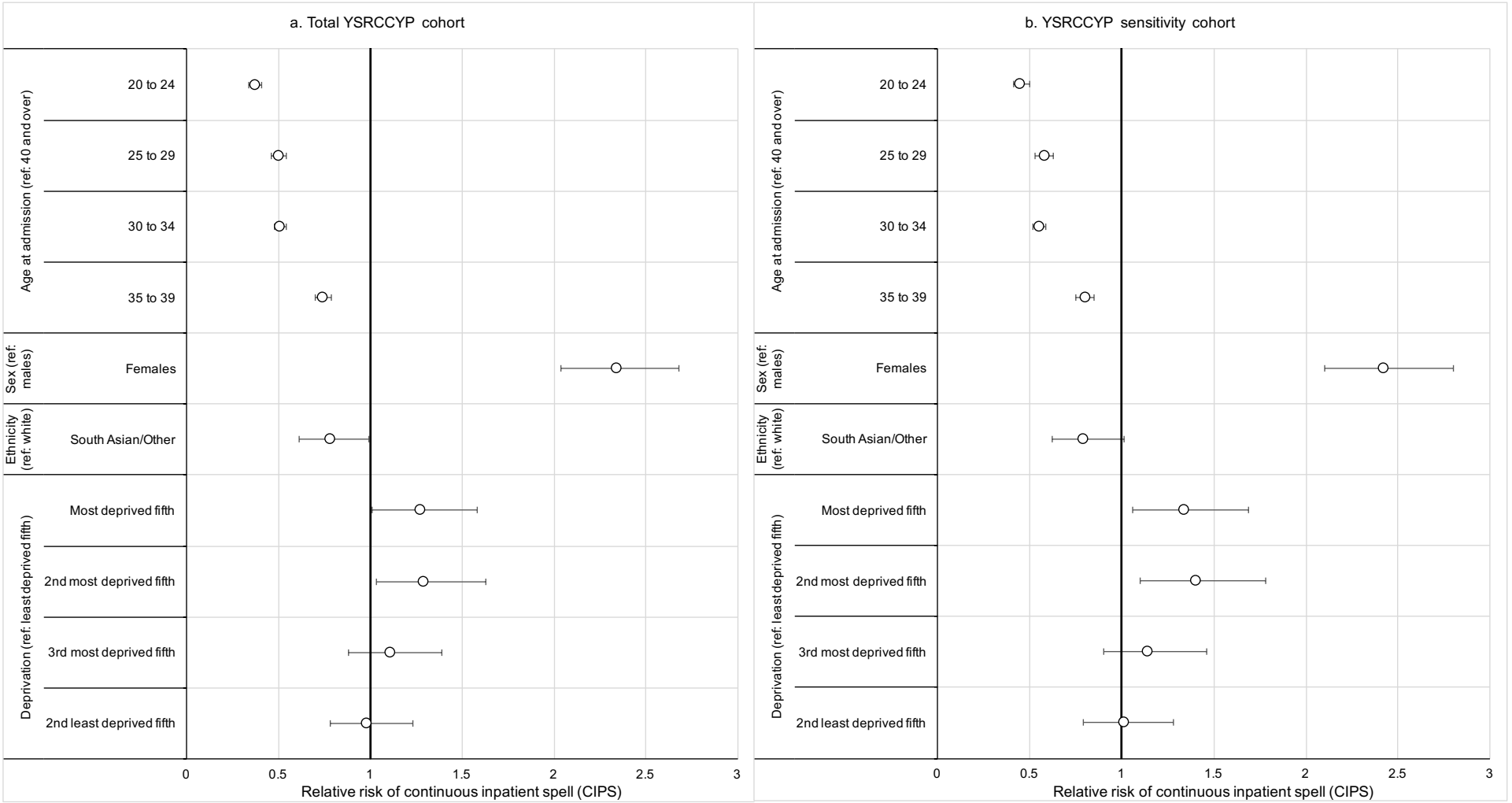


Figure 6.24: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals by age at CIPS – late cancer onset (a.) and equivalent sensitivity cohort (b.).

In late cancer onset, all age groups had significantly lower risk of CIPS compared with the 40 and over age group. The trend in the sensitivity cohort was similar (Figure 6.24).

Females had a significant increased risk of CIPS compared with males, particularly in late cancer onset, where the risk was more than double for females compared with males (2.34 (95%CI 2.04 to 2.68) (Figure 6.24).

No significant differences in risk of CIPS by ethnicity were found in early or late cancer onset.

In both early and late onset, there was a significantly higher risk of CIPS in the most deprived fifth compared with the least deprived fifth. In the sensitivity analysis, risk by deprivation groups were similar in late cancer onset. In early cancer onset, the most deprived fifth had a slightly higher relative risk than in the total cohort by 20%.

6.3.4.5 Inpatient admissions by cancer type.

In early cancer onset (Figure 6.25), leukaemias, CNS neoplasms, malignant bone tumours and soft tissue tumours had significantly higher risk of CIPS compared with the reference cancer type (neuroblastoma). The trends in relative risk by cancer type in the sensitivity cohorts were similar, with slightly lower risk for each cancer type.

In late cancer onset, there was no significant variation between cancer types. Lymphomas (0.6; 95% CI 0.42 to 0.87), germ cell tumours (0.41; 95% CI 0.28 to 0.59) and other malignant epithelial tumours (0.5; 95% CI 0.34 to 0.75) had significantly lower risk of CIPS compared with malignant bone tumours (Figure 6.26).

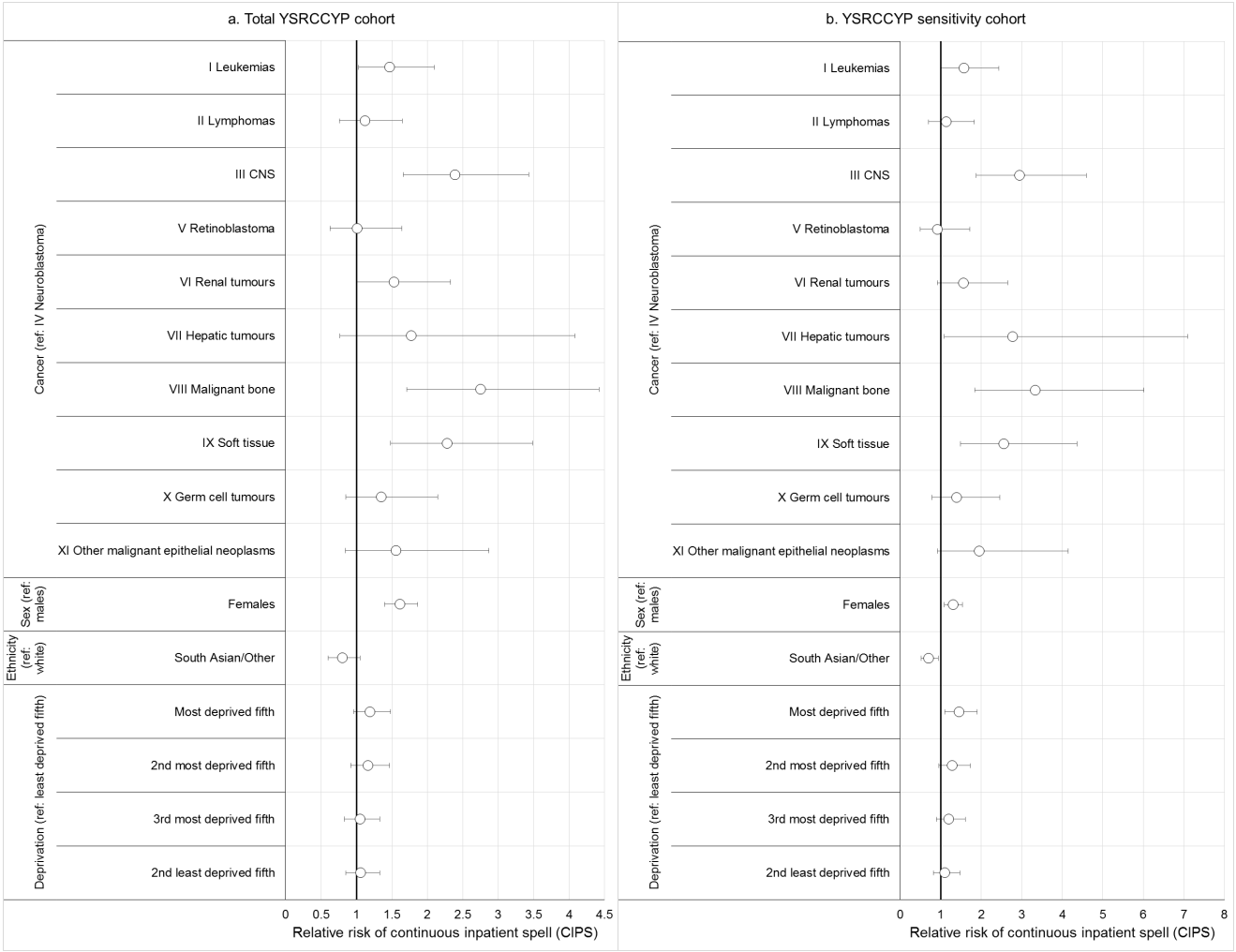


Figure 6.25: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals by cancer type – early cancer onset (a.) and equivalent sensitivity cohort (b.).

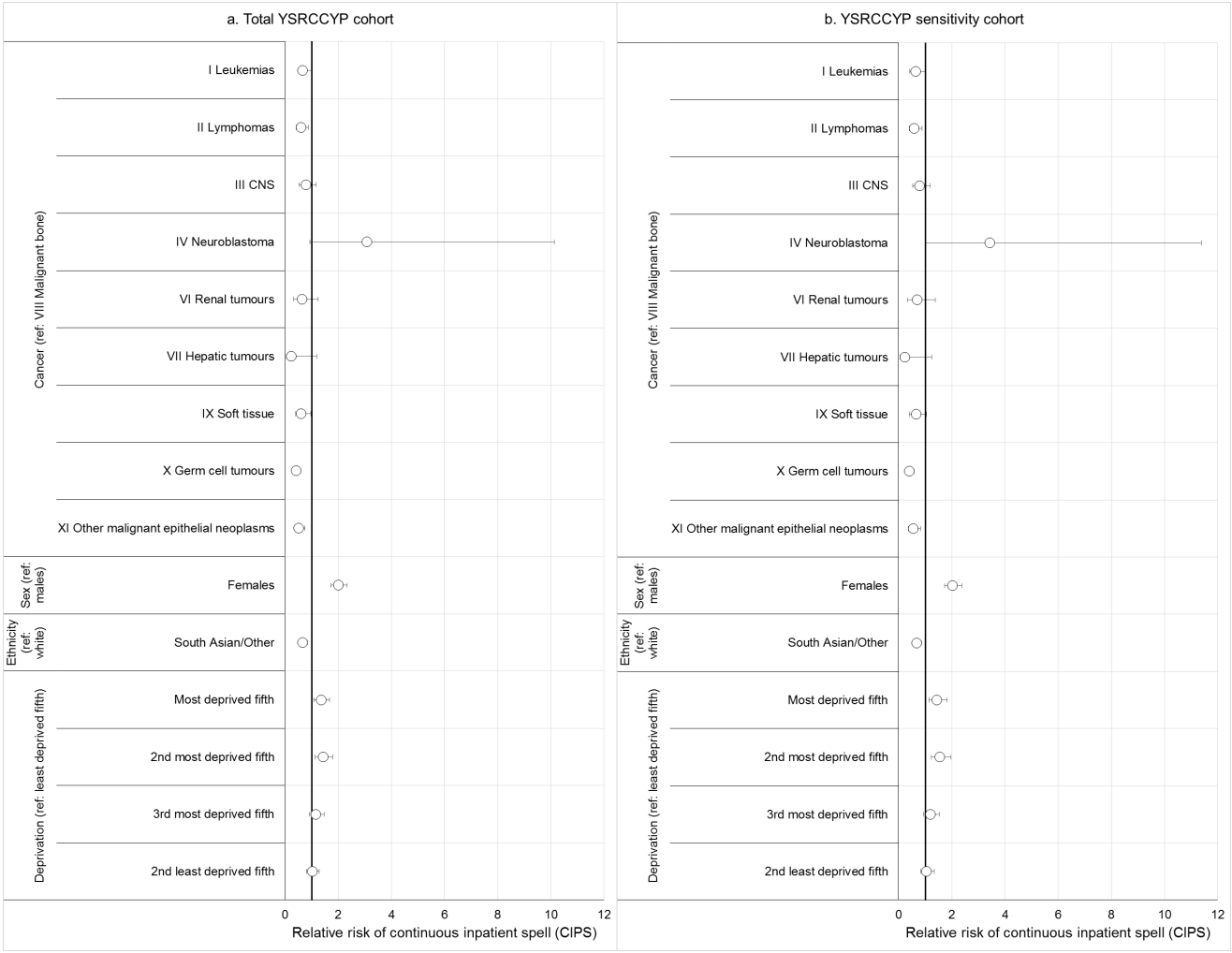


Figure 6.26: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals by cancer type – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.4.6 Inpatient admissions by primary diagnosis.

All primary diagnoses for CIPS had a significantly lower risk of CIPS compared with neoplasms. Certain infectious and parasitic diseases, diseases of the respiratory system, diseases of the skin and subcutaneous tissue and congenital malformations, deformations and chromosomal abnormalities had the lowest relative risks of CIPs compared with neoplasms in early and late cancer onset. Certain conditions originating in the perinatal period also had one of the five lowest relative risks of CIPS in early cancer onset. Mental and behavioural disorders had one of the five lowest relative risk of CIPS compared with neoplasms in late cancer onset.

Endocrine, nutritional and metabolic diseases and pregnancy, childbirth and the puerperium were within the top five primary diagnoses with the highest relative risk of CIPS compared with neoplasms in early and late cancer onset. Diseases of the nervous system were found to have one of the five highest risks of CIPS compared with neoplasms in both early (0.36; 95% CI 0.35 to 0.38) and late onset (0.39; 95% CI 0.36 to 0.42). Although mental and behavioural disorders had one of the lowest risks of CIPS in late cancer onset (0.22; 95%CI 0.19 to 0.25), this was shown to have one of the highest risks of CIPS compared with neoplasms in early cancer onset (0.63; 95% CI 0.58 to 0.69).

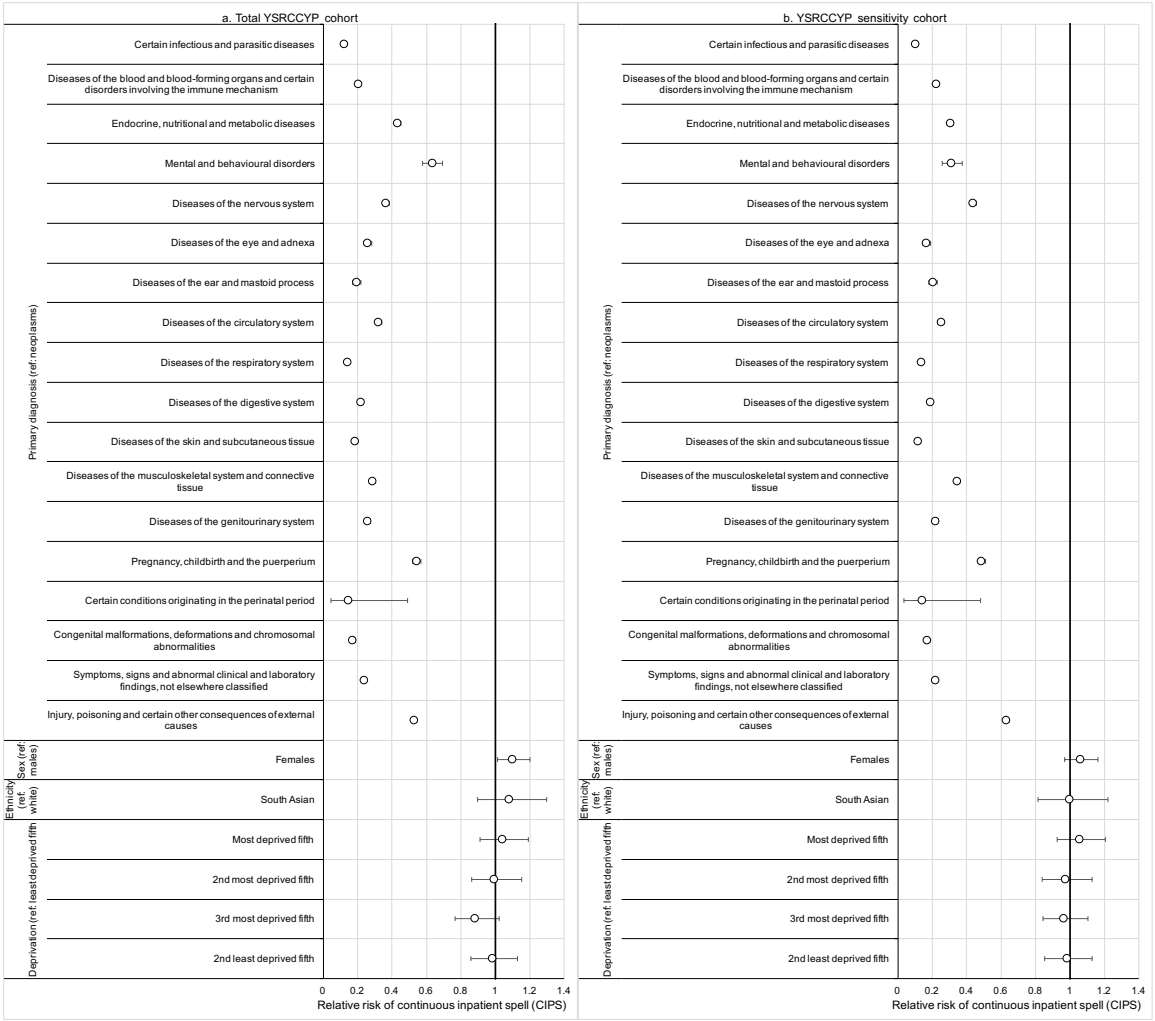


Figure 6.27: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals by primary diagnosis for admission – early cancer onset (a.) and equivalent sensitivity cohort (b.).

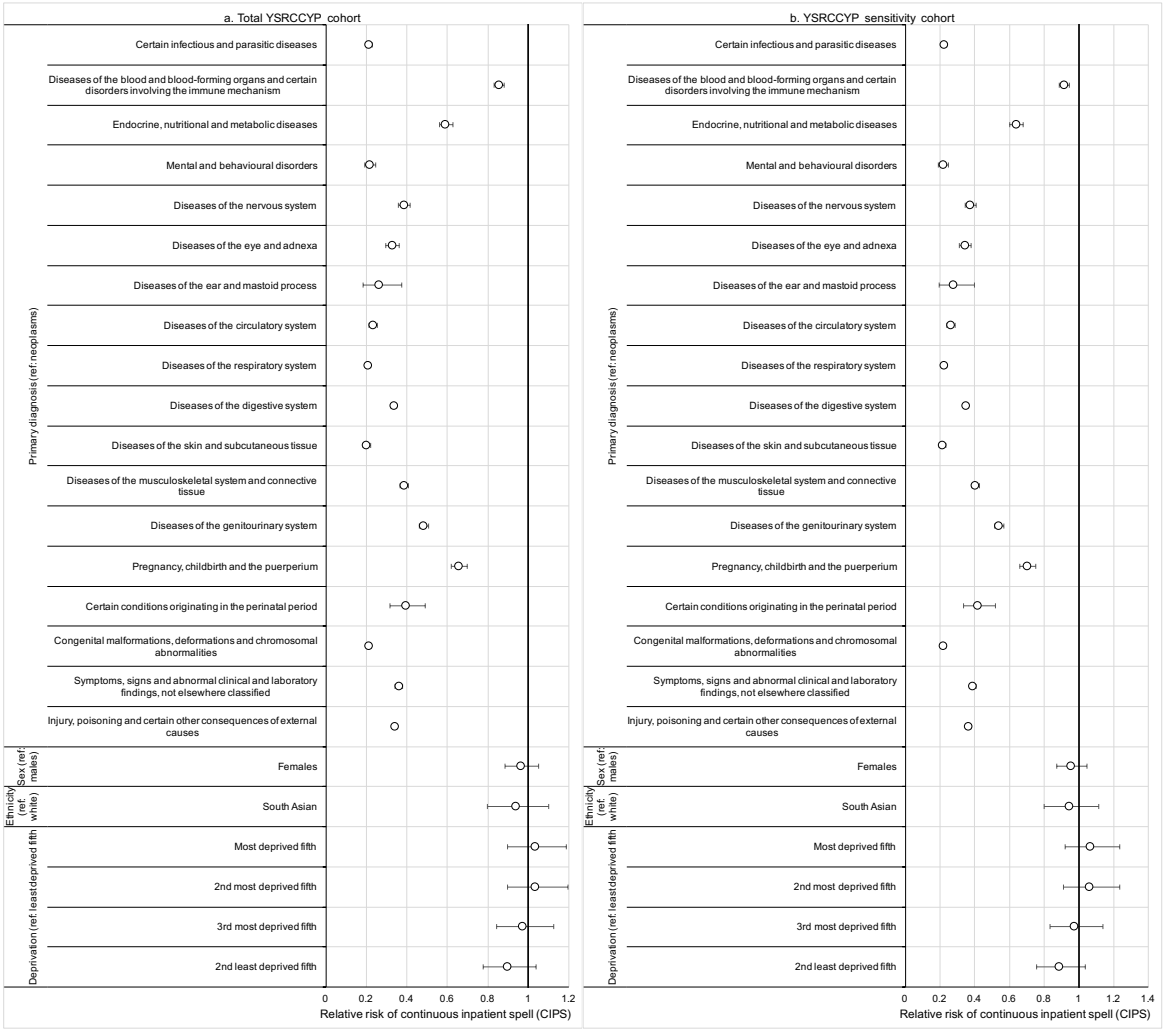


Figure 6.28: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals by primary diagnosis for admission – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.4.7 Inpatient admissions by treatment specialty.

All treatment specialties had a significantly lower risk of CIPS compared with oncology. Respiratory, oral health and ears/nose/throat treatment specialities had the lowest relative risks of CIPs compared with neoplasms in early and late cancer onset and in each of the equivalent sensitivity cohorts.

Neurology was one of the top three treatment specialities with the highest relative risk of CIPS compared with oncology in early and late cancer onset. Nephrology and endocrinology were also in the top three treatment specialities with the highest relative risk of CIPS compared with oncology in late cancer onset. In early cancer onset, the other two treatment specialities with the top three relative risk for CIPS were Maternity/Obstetrics/Gynaecology and circulatory.

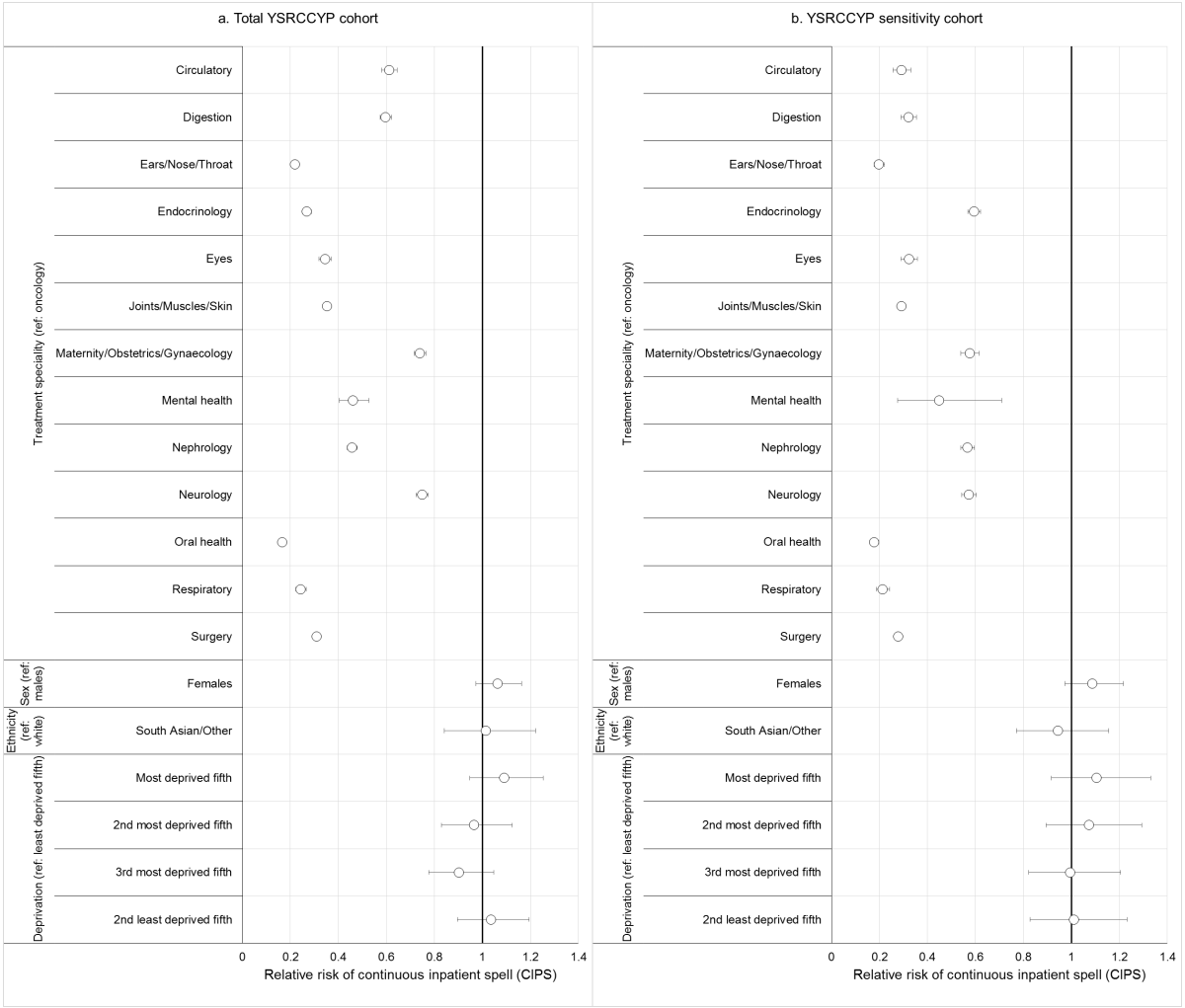


Figure 6.29: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals by treatment specialty – early cancer onset (a.) and equivalent sensitivity cohort (b.).

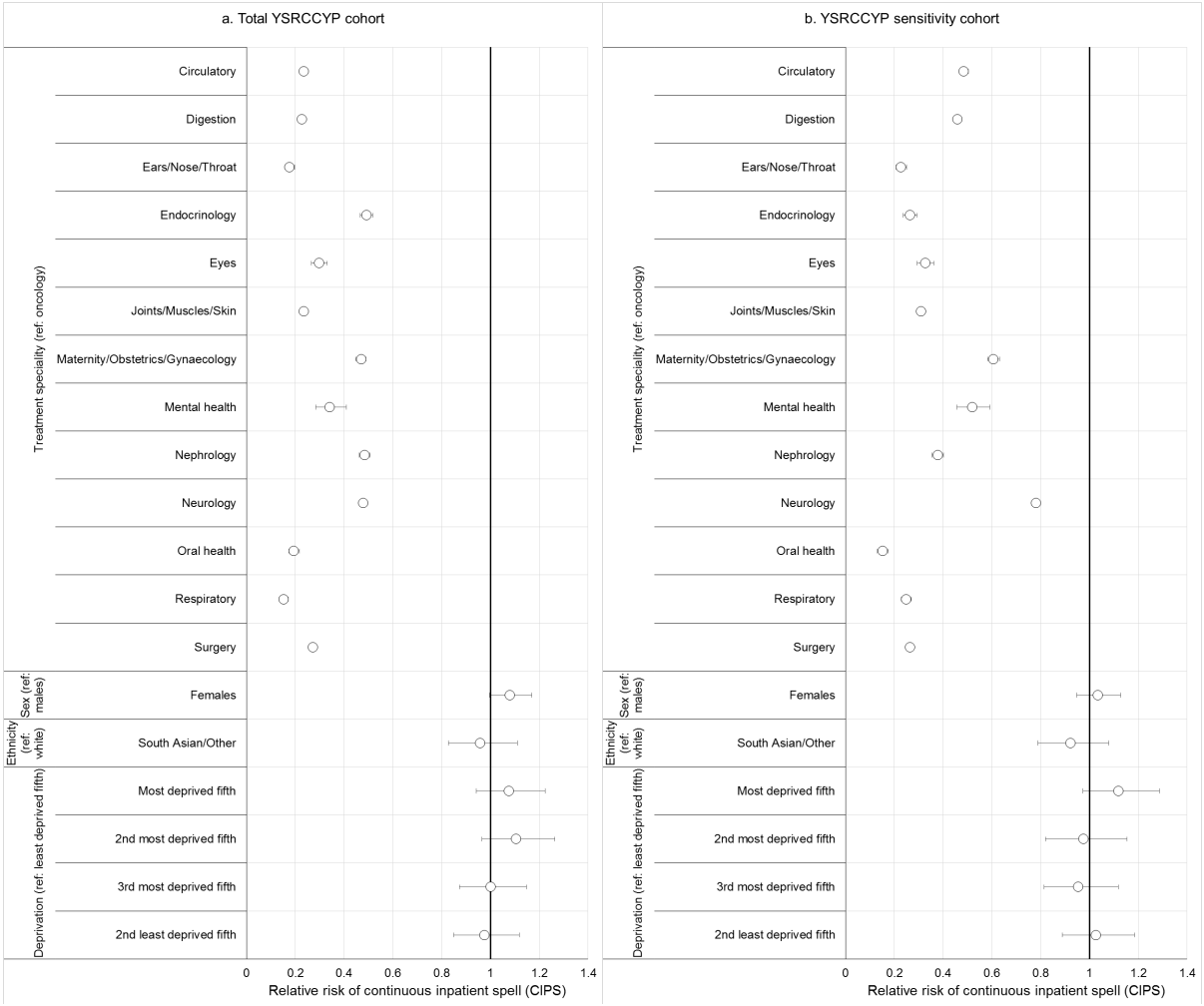


Figure 6.30: Relative risk of continuous inpatient spell (CIPS) from mixed effects Poisson model with 95% confidence intervals treatment specialty – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.4.8 Inpatient admission by mental health admission.

Of the 3,666 individuals with a CIPS, 404 (11%) had a mental health admission any time before a CIPS. There was a higher percentage of individuals with a mental health admission with late cancer onset (n=237; 13.1% of the late cancer onset total) compared with early cancer onset (n=167; 9% of the early cancer onset total). The number of individuals with a mental health admission in the most deprived group (n=121; 13.6% of the most deprived fifth total) was over two-fold of the least deprived fifth (n=50; 8.2% of the least deprived fifth total) (Table 6.13).

Table 6.13: Number of individuals with a mental health admission any time before a continuous inpatient spell (CIPS) by socio-demographic groups.

		Total individuals with a mental health admission before a CIPS			Total individuals with a CIPS
		N	% of group	% of total	
Age at cancer diagnosis	0 to 14 years (early onset)	167	9.0	4.6	1,848
	15 to 29 years (late onset)	237	13.1	6.5	1,812
Sex	Males	204	10.2	5.6	2,001
	Females	29	1.7	0.8	1,659
Ethnicity	White	315	11.1	8.6	2,835
	South Asian/Other	28	9.9	0.8	282
Deprivation	Least deprived fifth	50	8.2	1.4	610
	2nd least deprived fifth	70	10.0	1.9	699
	3rd most deprived fifth	71	10.7	1.9	661
	2nd most deprived fifth	78	11.9	2.1	653
	Most deprived fifth	121	13.6	3.3	891
Total		404	11.0	11.0	3,660

After other malignant epithelial neoplasms, individuals diagnosed with CNS neoplasms had the highest percentage of individuals with a mental health admission before a CIPS at 12.8% (n=87), followed by germ cell tumours (n=72; 12.7%). The lowest percentages were found in retinoblastoma (n=3; 4.3%), neuroblastoma (n=7; 8.8%) and leukaemias (n=63; 8.8%) (Table 6.14).

Table 6.14: Number of individuals with a mental health admission any time before a continuous inpatient spell (CIPS)by cancer type.

	Total individuals with a mental health admission before a CIPS			Total individuals with a CIPS
	N	% of group	% of total	
I Leukaemias	63	8.8	1.7	712
II Lymphomas	78	10.5	2.1	746
III CNS	87	12.8	2.4	680
IV Neuroblastoma	7	8.8	0.2	80
V Retinoblastoma	3	4.3	0.1	70
VI Renal tumours	13	8.6	0.4	152
VIII Malignant bone	18	11.5	0.5	156
IX Soft tissue	26	11.9	0.7	219
X Germ cell tumours	72	12.7	2.0	569
XI Other malignant epithelial neoplasms	36	14.5	1.0	249
Total	404	11.0	11.0	3,660

Multi-level logistic regression modelling for the overall cohort found that a previous mental health admission did not significant increase the odds of a CIPS (Figure 6.31).

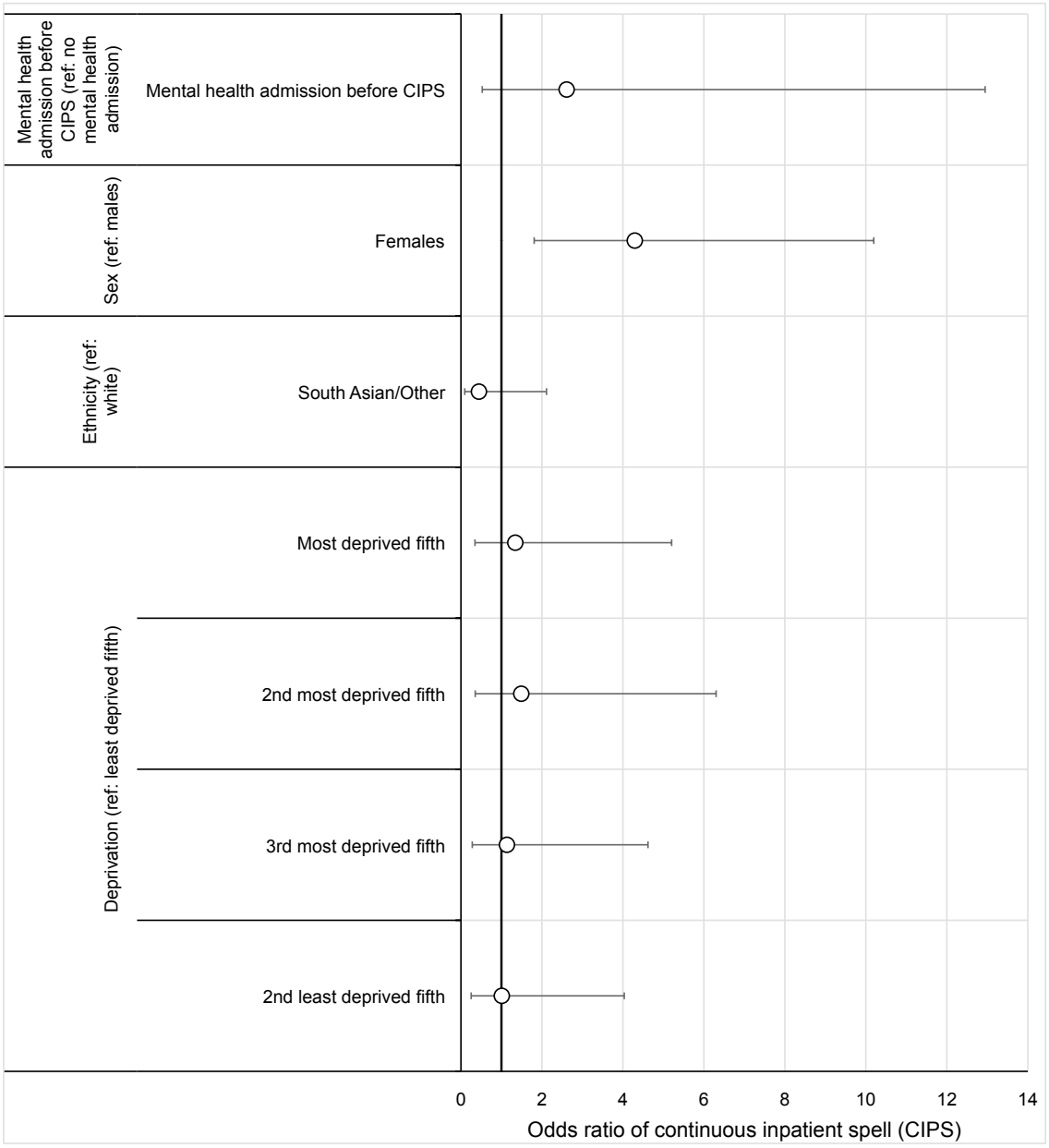


Figure 6.31: Odds ratio from mixed effects logistic regression model of continuous inpatient spell (CIPS) with 95% confidence intervals by previous mental health admission.

6.3.4.9 Inpatient admission by outpatient appointment attendance status.

In total, 2,566 individuals (54.2%) had a CIPS within 90 days of an outpatient appointment. The percentage of individuals with early cancer onset (n=1,307; 56.5%) was higher than in late cancer onset (n=1,259; 52%). The percentage of females with a CIPS was nearly 20% higher (n=1,263; 64.6%) compared with males (n=1,303; 46.9%). Percentages increased by deprivation group up to the second most deprived fifth with 57.4% (n=468) of individuals with a CIPS 90 days after an outpatient appointment (Table 6.15).

Table 6.15: Number of individuals with a continuous inpatient spell (CIPS) within 90 days of an outpatient appointment by socio-demographic groups.

		Total individuals with CIPS within 90 days of an outpatient appointment			Total individuals with an outpatient appointment
		N	% of group	% of total	
Age at cancer onset	0 to 14 years (early onset)	1,307	56.5	27.6	2,313
	15 to 29 years (late onset)	1,259	52.0	26.6	2,422
Sex	Males	1,303	46.9	27.5	2,780
	Females	1,263	64.6	26.7	1,955
Ethnicity	White	1,986	53.1	41.9	3,740
	South Asian/Other	199	50.5	4.2	394
Deprivation	Least deprived fifth	405	49.2	8.6	823
	2nd least deprived fifth	507	54.7	10.7	927
	3rd most deprived fifth	450	54.3	9.5	829
	2nd most deprived fifth	468	57.4	9.9	815
	Most deprived fifth	637	55.8	13.5	1,142
Total		2,566	54.2	54.2	4,735

Individuals diagnosed with CNS neoplasms (n=492; 67.2%), malignant bone tumours (n=117; 66.1%) and hepatic tumours (n=14; 60.9%) had the highest percentage of individuals with a CIPS within 90 days of an outpatient appointment. The lowest percentages were found in germ cell tumours (n=366; 44.5%), retinoblastoma (n=45; 45%) and neuroblastoma (n=54; 48.6%) (Table 6.16).

Table 6.16: Number of individuals with a continuous inpatient spell (CIPS) within 90 days of an outpatient appointment by cancer type.

	Total individuals with CIPS within 90 days of an outpatient appointment			Total individuals with an outpatient appointment
	N	% of group	% of total	
I Leukaemias	504	52.7	10.6	956
II Lymphomas	516	50.2	10.9	1028
III CNS	492	67.2	10.4	732
IV Neuroblastoma	54	48.6	1.1	111
V Retinoblastoma	45	45.0	1.0	100
VI Renal tumours	110	57.0	2.3	193
VII Hepatic tumours	14	60.9	0.3	23
VIII Malignant bone	117	66.1	2.5	177
IX Soft tissue	152	60.6	3.2	251
X Germ cell tumours	366	44.5	7.7	823
XI Other malignant epithelial neoplasms	190	56.9	4.0	334
Total	2,566	54.2	54.2	4,735

There were 28,192 (23%) of outpatient appointments where a CIPS occurred within 90 days. Of these 28,192 outpatient appointments, 6.6% (n=1,860) had a DNA status. This is lower compared to the overall outpatient cohort at 10.3% (Table 6.4). The percentage of DNA appointments in outpatient appointments with no CIPS after 90 days was higher at 11.4% (n=10,731) (Table 6.17).

By cancer type, germ cell tumours had the highest percentage of DNA appointments where a CIPS occurred within 90 days of the appointment at 9.2% (n=189). This was followed by retinoblastoma at 8.8% (n=27) and renal tumours at 7.5% (n=104) (Table 6.18).

Mixed effects logistic regression modelling found that individuals who did not attend an outpatient appointment had a significantly lower odds of a CIPS after 90 days compared with those who attended outpatient appointments by around 50%. A similar result was found in the sensitivity cohort (Figure 6.32).

Table 6.17: Number of outpatient appointments and continuous inpatient spells (CIPS) by socio-demographic groups.

		Total outpatient appointments								Total
		No CIPS				CIPS within 90 days after an outpatient appointment				
		Did not attend		Attended		Did not attend		Attended		
		N	%	N	%	N	%	N	%	
Age at cancer diagnosis	0 to 14 years (early onset)	5,600	7.9	48,764	69.2	1,035	1.5	14,975	21.2	70,476
	15 to 29 years (late onset)	5,131	9.9	34,583	66.6	825	1.6	11,357	21.9	51,946
Sex	Males	5,929	9.9	42,284	70.7	803	1.3	10,739	18.0	59,814
	Females	4,802	7.7	41,063	65.6	1,057	1.7	15,593	24.9	62,608
Ethnicity	White	8,302	8.7	64,710	68.1	1,417	1.5	20,491	21.6	95,015
	South Asian/Other	1,003	10.4	6,389	66.2	203	2.1	2,049	21.2	9,650
Deprivation	Least deprived fifth	1,406	6.7	15,178	71.8	215	1.0	4,313	20.4	21,135
	2nd least deprived fifth	1,596	6.8	16,399	69.5	289	1.2	5,308	22.5	23,612
	3rd most deprived fifth	1,766	8.6	14,277	69.4	287	1.4	4,192	20.4	20,564
	2nd most deprived fifth	2,076	9.2	15,097	66.9	419	1.9	4,937	21.9	22,564
	Most deprived fifth	3,448	11.5	19,419	64.8	584	1.9	6,479	21.6	29,955
Total		10,731	8.8	83,347	68.1	1,860	1.5	26,332	21.5	122,422

Table 6.18: Number of outpatient appointments and continuous inpatient spells (CIPS) by cancer type.

	Total outpatient appointments								Total
	No CIPS				CIPS within 90 days after an outpatient appointment				
	Did not attend		Attended		Did not attend		Attended		
	N	%	N	%	N	%	N	%	
I Leukaemias	2,466	8.8	18,908	67.8	375	1.3	6,099	21.9	27,876
II Lymphomas	2,299	9.8	15,236	64.8	433	1.8	5,510	23.4	23,502
III CNS	1,509	5.8	17,755	68.7	382	1.5	6,154	23.8	25,833
IV Neuroblastoma	315	10.0	2,423	77.0	27	0.9	379	12.0	3,146
V Retinoblastoma	331	12.3	2,046	76.0	27	1.0	281	10.4	2,693
VI Renal tumours	468	8.9	3,382	64.4	104	2.0	1,280	24.4	5,250
VII Hepatic tumours	31	6.1	392	77.2	4	0.8	81	15.9	508
VIII Malignant bone	379	7.5	3,570	70.2	77	1.5	1,055	20.7	5,087
IX Soft tissue	539	7.6	4,875	68.4	92	1.3	1,613	22.6	7,127
X Germ cell tumours	1,472	12.1	8,641	71.0	189	1.6	1,858	15.3	12,175
XI Other malignant epithelial neoplasms	902	10.2	5,858	66.3	146	1.7	1,911	21.6	8,829
Total	10,731	8.8	83,347	68.1	1,860	1.5	26,332	21.5	122,422

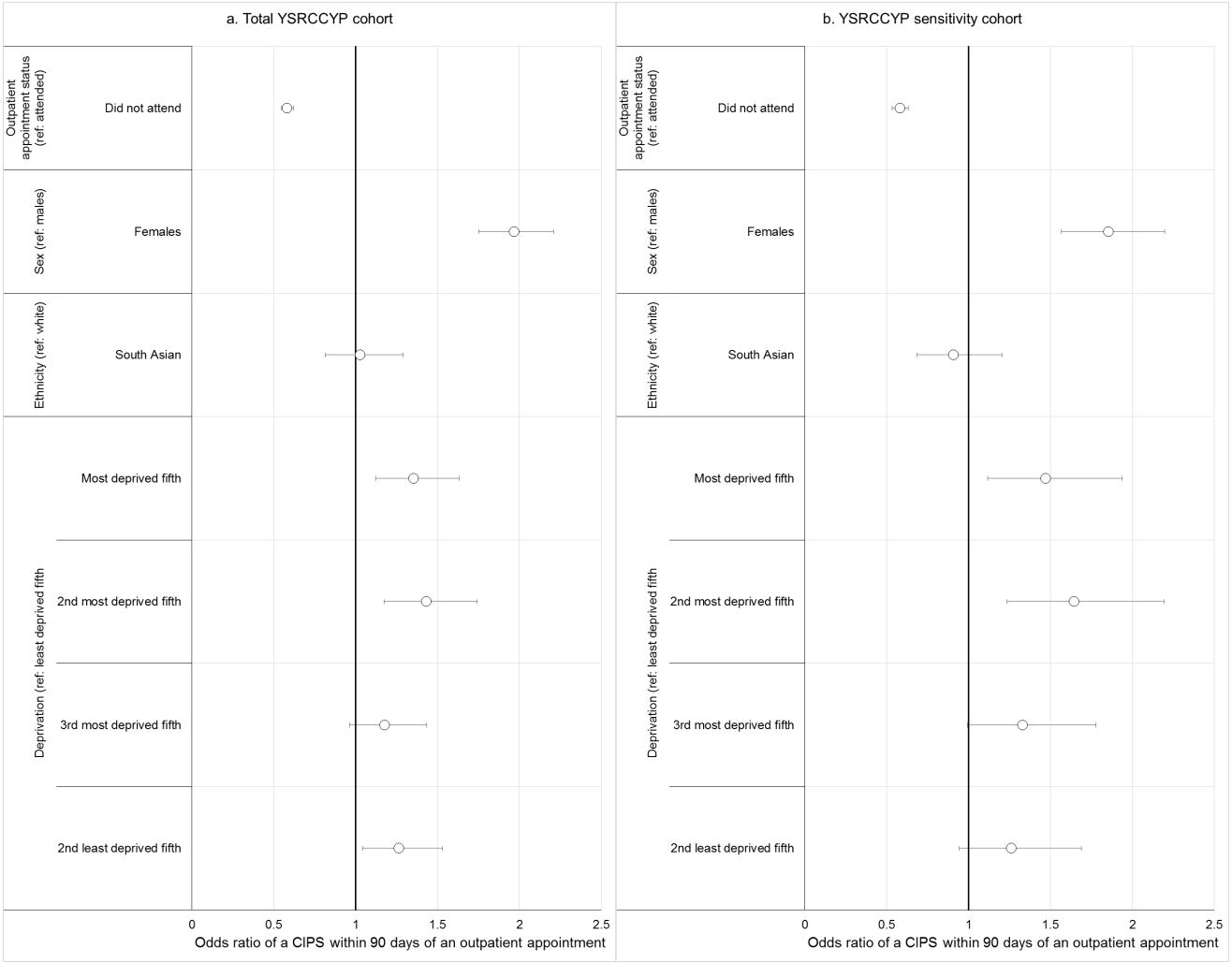


Figure 6.32: Odds ratio from mixed effects logistic regression model of a continuous inpatient spell (CIPS) within 90 days of an outpatient appointment with 95% confidence intervals (a.) and equivalent sensitivity cohort (b.).

6.3.5 Accident and emergency (A&E) data analysis

6.3.5.1 Demographics.

There were 3,034 individuals (57.3% of eligible individuals) who were matched on the HES A&E dataset. The percentages of the matched YSRCCYP dataset by age at cancer onset group, sex and deprivation were similar to the overall YSRCCYP cohort. By ethnicity, the percentage of individuals with white ethnic origin is slightly higher at 78.6% (Figure 6.33) compared with 68.9% in the overall YSRCCYP cohort (Figure 6.1).

The cancer type with the highest number of individuals with an A&E attendance was lymphoma (n=642; 21.2%), followed by leukaemia (n=602; 19.8%) and germ cell tumours (n=547, 18%). Hepatic tumours were the least likely cancer diagnosis in individuals with an A&E attendance (n=15) after the other and unspecified group (n=6).

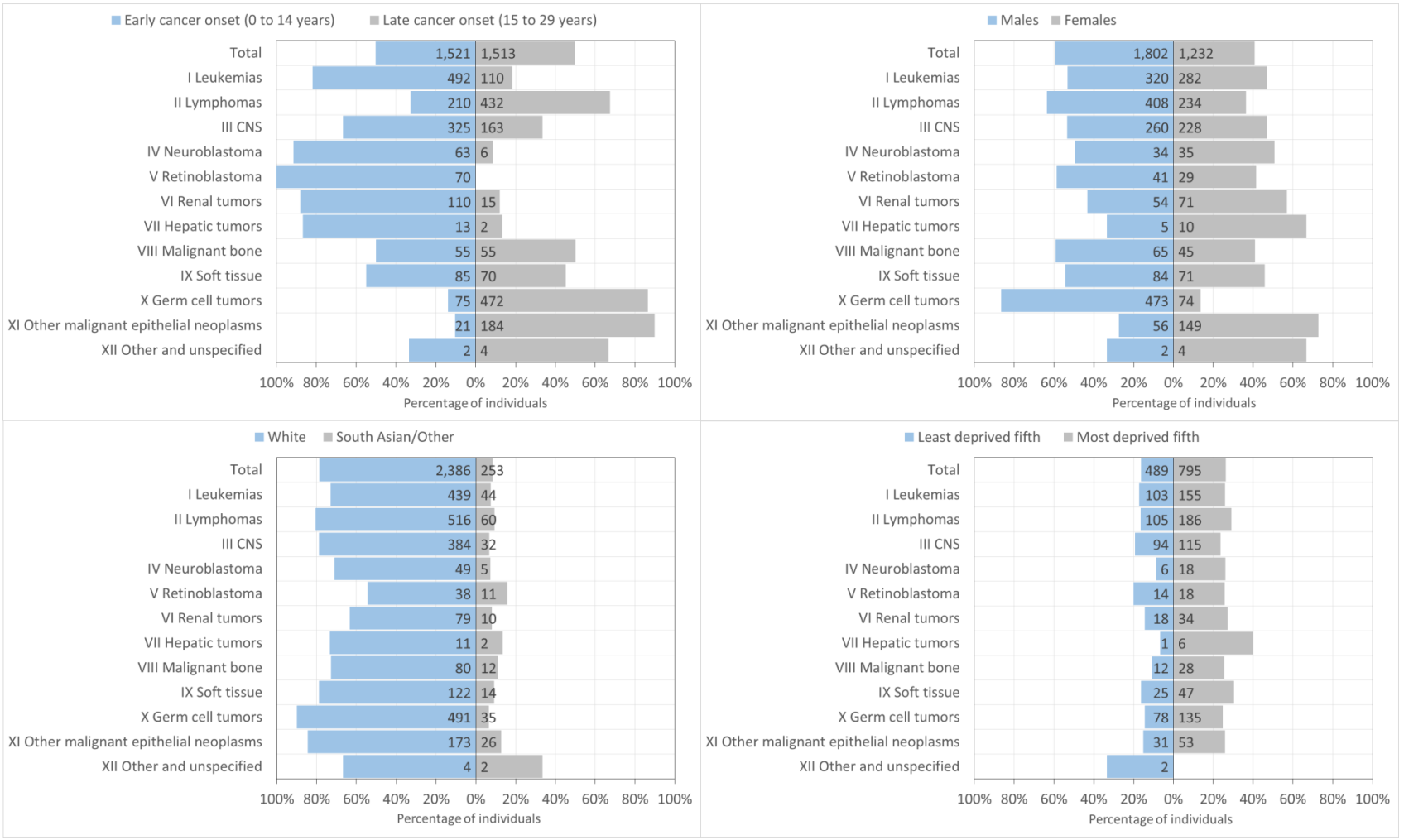


Figure 6.33: Percentage (and number) of individuals linked to accident and emergency (A&E) data by cancer type and socio-demographic groups.

6.3.5.2 Total accident and emergency (A&E) attendances by socio-demographic groups, cancer type A&E arrival mode.

The total number of A&E attendances was 9,985. Over three-quarters of A&E attendances arrived via ambulance (n=7,778; 77.9%). The mean number of A&E attendances for an individual was 3.3 (range 1 to 79). There were over twice as many A&E attendances in the most deprived fifth (n=2,925; 29.3%) compared with the least deprived fifth (n=1,426; 14.3%) (Table 6.19).

The total number of A&E attendances was greatest after the transitional care period (n=4,699; 47.1%). There was a total of 4,048 (40.5%) attendances during and 1,038 (10.4%) attendances before the transitional care period. By 5-year age bands, the total number of A&E attendances increased for each category, with the highest total for the 35 to 39-year age group. The age group with the highest mean of A&E attendances was the 40 and over group at 2.9 (range 1 to 38) (Table 6.19).

Table 6.19: Descriptive statistics of accident and emergency (A&E) attendances by socio-demographic groups, age at A&E attendance and A&E arrival mode.

		Total A&E attendances				
		N	% of total	Mean	Median (range)	Standard deviation
Age at cancer diagnosis	0 to 14 years (early onset)	5,462	54.7	3.6	2 (1 to 66)	4.8
	15 to 29 years (late onset)	4,523	45.3	3.0	2 (1 to 53)	3.6
Sex	Males	5,772	57.8	3.2	2 (1 to 79)	4.3
	Females	4,213	42.2	3.4	2 (1 to 66)	4.8
Ethnicity	White	7,651	76.6	3.2	2 (1 to 79)	4.1
	South Asian/Other	875	8.8	3.5	2 (1 to 49)	4.6
Deprivation	Least deprived fifth	1,426	14.3	2.9	2 (1 to 39)	3.4
	2nd least deprived fifth	1,604	16.1	2.8	2 (1 to 28)	2.8
	3rd most deprived fifth	1,601	16.0	3.1	2 (1 to 63)	4.6
	2nd most deprived fifth	2,146	21.5	3.9	2 (1 to 51)	5.4
	Most deprived fifth	2,925	29.3	3.7	2 (1 to 79)	5.3
Age at A&E admission	5 to 9	300	3.0	1.9	1 (1 to 12)	1.7
	10 to 14	738	7.4	2.2	1 (1 to 16)	2.1
	15 to 19	1,217	12.2	2.5	2 (1 to 50)	3.5
	20 to 24	1,512	15.1	2.6	2 (1 to 37)	3.4
	25 to 29	1,519	15.2	2.3	2 (1 to 46)	2.7
	30 to 34	1,581	15.8	2.2	1 (1 to 52)	2.8
	35 to 39	1,588	15.9	2.4	1 (1 to 35)	2.9
	40 and over	1,530	15.3	2.9	2 (1 to 38)	4.0
A&E arrival mode	Ambulance	7,778	77.9	4.1	2 (1 to 79)	6.6
	Other	2,119	21.2	3.7	3 (1 to 9)	2.5
Total		9,985	100.0	3.3	2 (1 to 79)	4.5

Individuals diagnosed with leukaemias, lymphomas and CNS neoplasms had the highest total of A&E attendances. The cancer types with the highest mean A&E attendances per individual were renal tumours, CNS neoplasms and soft tissue tumours. The cancer types with the lowest mean A&E attendances per individual were malignant bone tumours, germ cell tumours and lymphomas (Table 6.20).

Table 6.20: Descriptive statistics of accident and emergency (A&E) attendances by cancer type.

	Total A&E attendances				
	N	**% of total**	**Mean**	**Median (range)**	**Standard deviation**
I Leukaemias	1,979	19.8	3.3	2 (1 to 35)	3.4
II Lymphomas	1,958	19.6	3.0	2 (1 to 39)	3.8
III CNS	1,817	18.2	3.7	2 (1 to 63)	5.9
IV Neuroblastoma	239	2.4	3.5	2 (1 to 21)	3.4
V Retinoblastoma	228	2.3	3.3	2 (1 to 30)	4.3
VI Renal tumours	526	5.3	4.2	3 (1 to 66)	7.3
VII Hepatic tumours	46	0.5	3.1	2 (1 to 7)	2.1
VIII Malignant bone	319	3.2	2.9	2 (1 to 19)	2.6
IX Soft tissue	569	5.7	3.7	2 (1 to 25)	4.0
X Germ cell tumours	1,576	15.8	2.9	2 (1 to 79)	4.4
XI Other malignant epithelial neoplasms	703	7.0	3.4	2 (1 to 53)	4.9
Total	9,985	100.0	3.3	2 (1 to 79)	4.5

6.3.5.3 Incidence rates for accident and emergency (A&E) attendances.

The overall incidence rate was 175.7 per 1,000 person-years (95% CI 172.3 to 179.2 per 1,000 person-years), 162.6 per 1,000 person-years (95% CI 158.3 to 167 per 1,000 person-years) for early cancer onset (Figure 6.34) and 194.6 per 1,000 person-years (95% CI 189 to 200.4 per 1,000 person-years) for late cancer onset (Figure 6.35).

There were no statistically significant differences in A&E attendance incidence rates between the overall incidence rates with males or females in early (Figure 6.34) and late cancer onset (Figure 6.35).

In early cancer onset, the incidence rate for South Asian/Other ethnicity (331 per 1,000 person-years; 95% CI 303 to 361.6 per 1,000 person-years) was significantly higher than for white ethnicity (242 per 1,000 person-years; 95% CI 234.1 to 250.1 per 1,000 person-years) by around 40% (incidence rate for unknown ethnicity for early cancer onset was 82.8 per 1,000 person-years (95% CI 78.7 to 87.2 per 1,000 person-years)) (Figure 6.34). In late cancer onset, the

difference in A&E incidence rate for South Asian/Other ethnicity (224.4 per 1,000 person-years; 95% CI 203 to 248 per 1,000 person-years) was around 30% higher compared with white ethnicity (192.8 per 1,000 person-years; 95% CI 187.1 to 198.8 per 1,000 person-years) (Figure 6.35).

Analysis by deprivation groups showed the two most deprived groups had significantly higher A&E attendance incidence rate compared with the three least deprived groups in early and late cancer onset.

The age groups before the transitional care period had the lowest incidence rates for A&E attendance in early cancer onset and were significantly lower than the age groups during and after the transitional care period. Incidence rates were highest in the 40 and over group in early (240.2 per 1,000 person-years; 95% CI 215.7 to 267.5 per 1,000 person-years) and late cancer onset (252.2 per 1,000 person-years; 95% CI 238.3 to 266.9 per 1,000 person-years).

In the early cancer onset cohort, lymphomas (127.5 per 1,000 person-years; 95% CI 118.1 to 137.8 per 1,000 person-years), malignant bone tumours (134.2 per 1,000 person-years; 95% CI 115.8 to 155.4 per 1,000 person-years) and soft tissue tumours (139.2 per 1,000 person-years; 95% CI 124.9 to 155.2 per 1,000 person-years) had significantly lower A&E attendance incidence compared with the overall early cancer onset A&E incidence rate. CNS neoplasms (198 per 1,000 person-years; 95% CI 187.6 to 208.9 per 1,000 person-years), renal tumours (197.6 per 1,000 person-years; 95% CI 180.8 to 215.9 per 1,000 person-years), hepatic tumours (267.3 per 1,000 person-years; 95% CI 197.5 to 361.7 per 1,000 person-years) and germ cell tumours (188.7 per 1,000 person-years; 95% CI 168 to 212 per 1,000 person-years) had significantly higher A&E attendance incidence compared with the total early cancer onset A&E incidence rate (Figure 6.34).

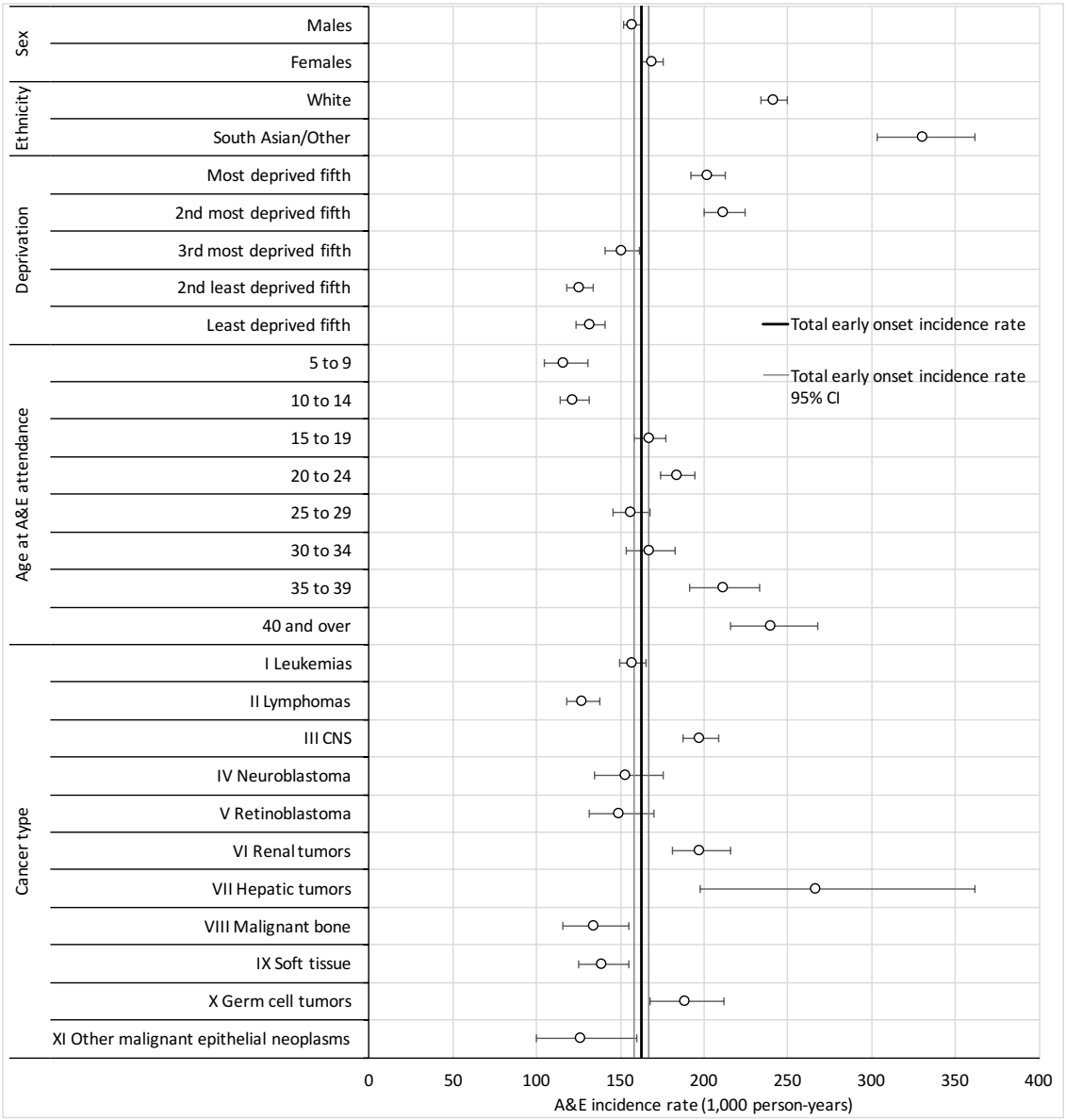


Figure 6.34: Incidence rate per 1,000 person-years for accident and emergency (A&E) attendances - early cancer onset.

In the late onset cohort, renal tumours (124.5 per 1,000 person-years; 95% CI 90.2 to 171.8 per 1,000 person-years) and germ cell tumours (174 per 1,000 person-years; 95% CI 164.7 to 183.7 per 1,000 person-years) had significantly lower A&E attendance incidence rates compared with the total late onset rate. CNS neoplasms (235 per 1,000 person-years; 95% CI 215.2 to 256.7 per 1,000 person-years), neuroblastomas (477.1 per 1,000 person-years; 95% CI 311.1 to 731.7 per 1,000 person-years) and other malignant epithelial neoplasms (236.7 per 1,000 person-years; 95% CI 219 to 255.9 per 1,000 person-years) had significantly higher incidence of A&E attendances compared with the overall late onset rate (Figure 6.35).

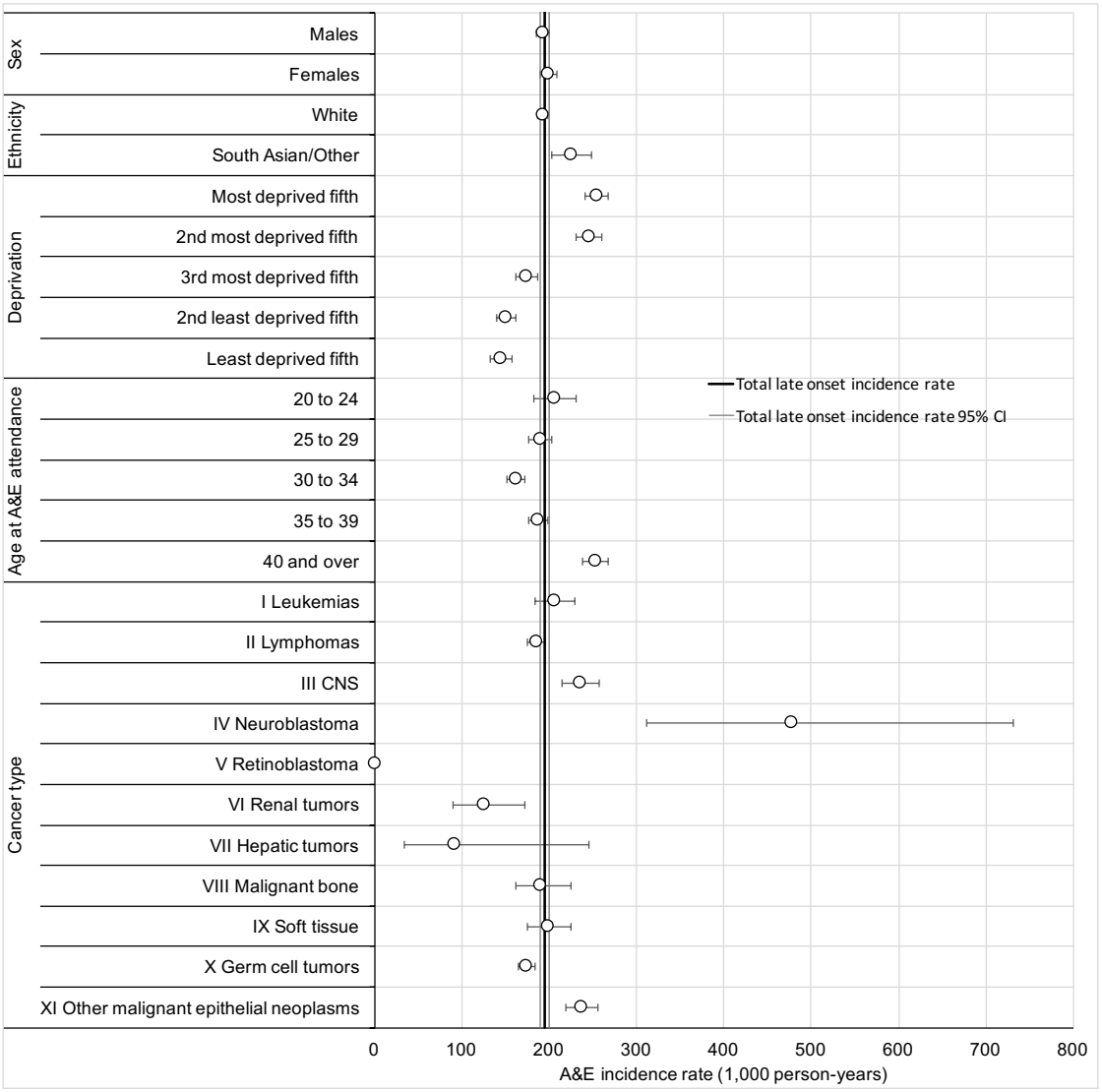


Figure 6.35: Incidence rate per 1,000 person-years for accident and emergency (A&E) attendances - late cancer onset cancer.

6.3.5.4 Accident and emergency (A&E) attendance by age at attendance.

Mixed effects Poisson modelling was used to assess relative risk of an A&E attendance by age at attendance. For the sensitivity analysis, models were run only for individuals matched on the A&E dataset who were diagnosed since 1st April 2002.

In early cancer onset, before the transitional care period, the risk of an A&E attendance in the 5 to 9-year age group was significantly lower compared with the risk of attending A&E in the 10 to 14-year age group. The age groups during and after the transitional care period had significantly higher risk of an A&E attendance compared with the 10 to 14-year age group, with an increasing trend by 5-year age category. However, this is in contrast to the sensitivity cohort, where it was found that either there was no significant difference in A&E

attendance compared with the 10 to 14-year age group or A&E attendance was significantly lower. There were no individuals from the 30 to 34-year age group included in the sensitivity cohort (Figure 6.36).

In late cancer onset, all age groups had significantly lower risk of attending A&E compared with the 40 and over group. However, the sensitivity analysis showed the opposite results where all age groups had significantly higher risk of attending A&E compared with the 40 and over group (Figure 6.37).

In both early and late cancer onset, compared with males and white ethnicity, no significant differences in risk of A&E attendance was found for females and South Asian/Other ethnicity, respectively.

There was a significantly higher risk of attending A&E in the most deprived and second most deprived fifths compared with the least deprived fifth in early and late cancer onset. This was also found in the sensitivity cohort in early cancer onset. However, in late cancer onset, the risk of attending A&E was only significantly higher in the most deprived fifth compared with the least deprived fifth.

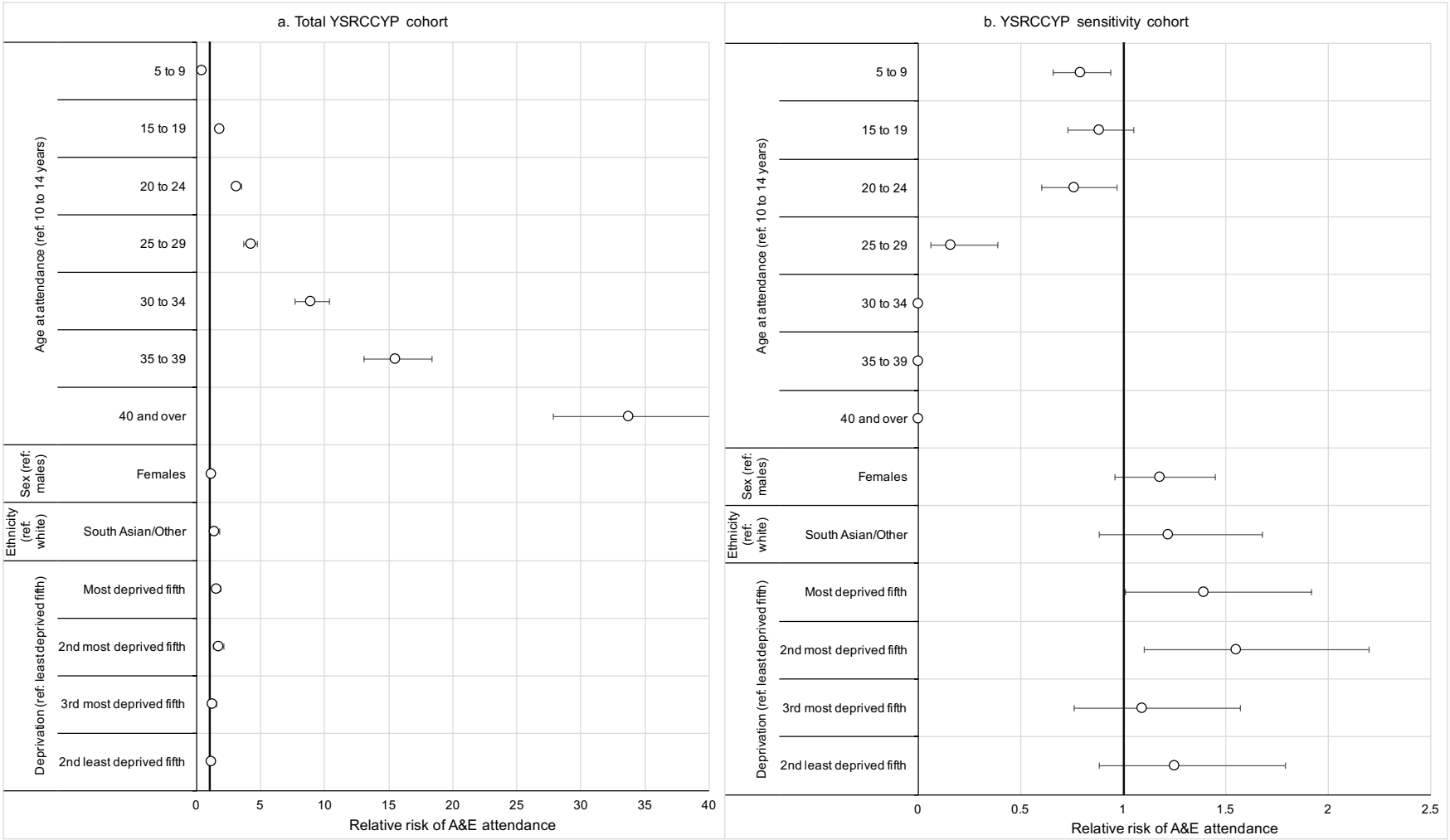


Figure 6.36: Relative risk of accident and emergency (A&E) attendance from mixed effects Poisson model with 95% confidence intervals by age at A&E attendance – early cancer onset (a.) and equivalent sensitivity cohort (b.).

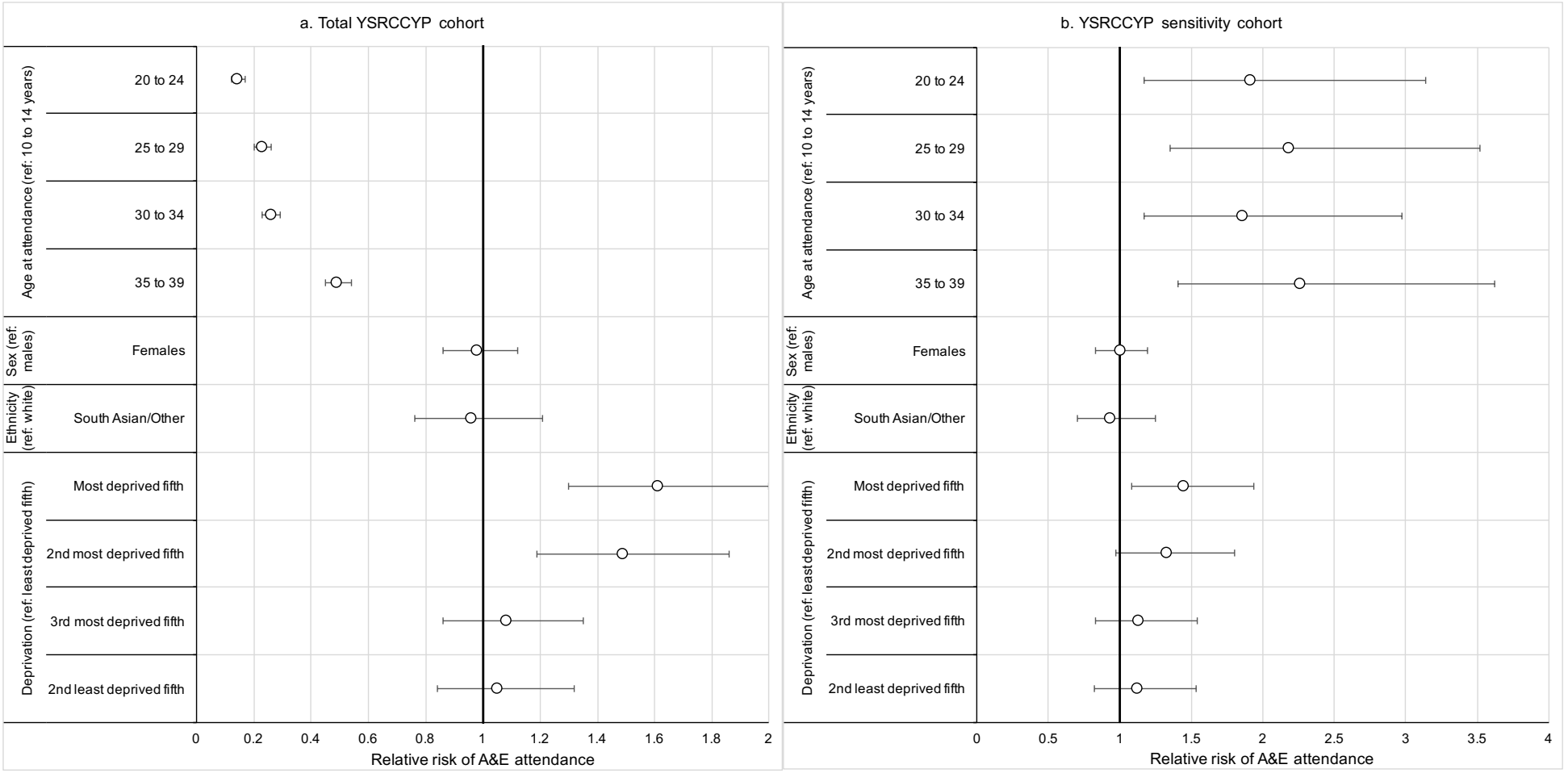


Figure 6.37: Relative risk of accident and emergency (A&E) attendance from mixed effects Poisson model with 95% confidence intervals – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.5.5 Accident and emergency (A&E) attendance by cancer type.

No significant differences were found in risk of A&E attendance by any cancer type compared with the reference cancer type and in early (Figure 6.38) and late cancer onset (Figure 6.39). This was also found in the equivalent sensitivity cohorts.

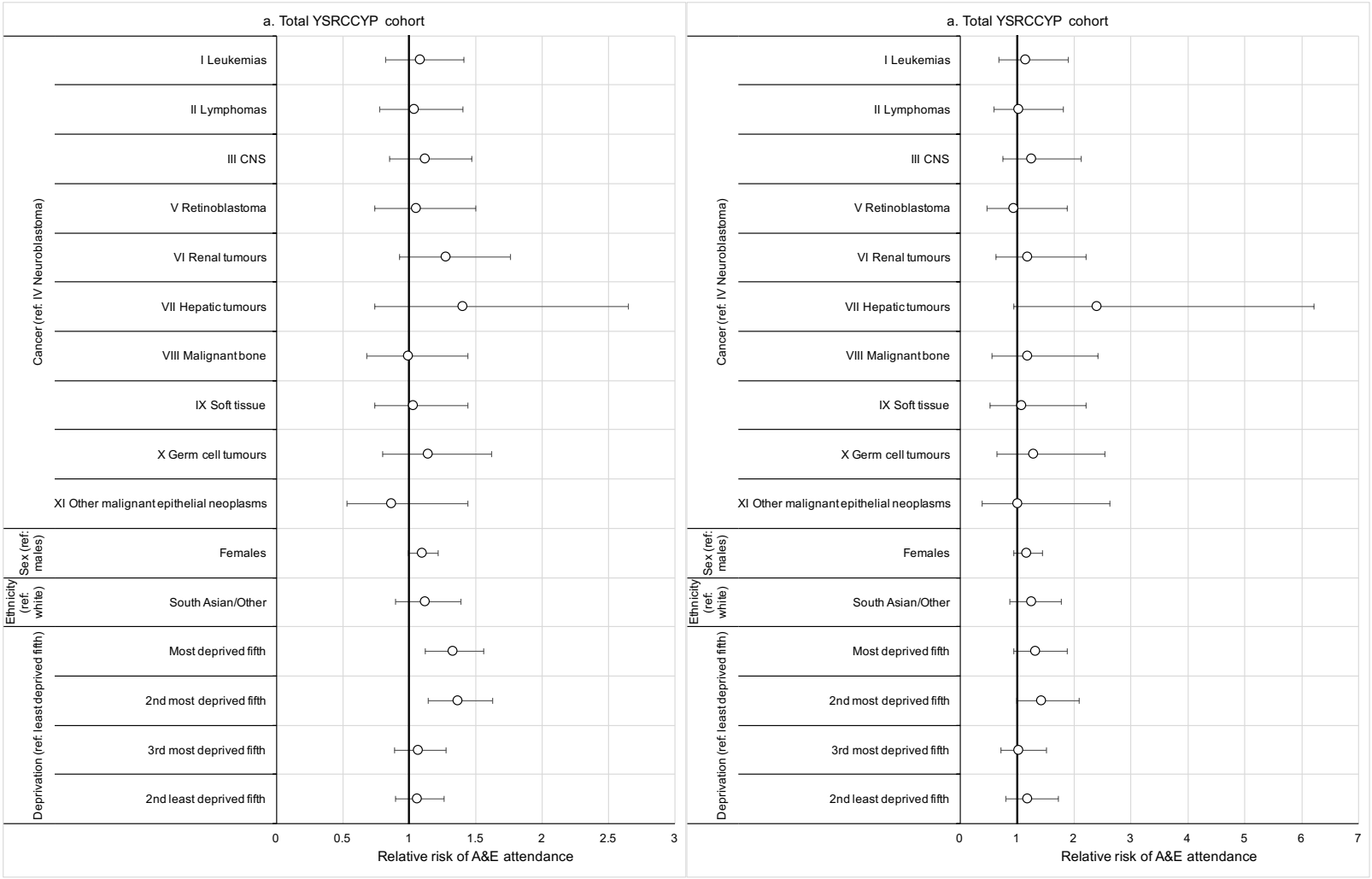


Figure 6.38: Relative risk of accident and emergency (A&E) attendance from mixed effects Poisson model with 95% confidence intervals by cancer type – early cancer onset (a.) and equivalent sensitivity cohort (b.).

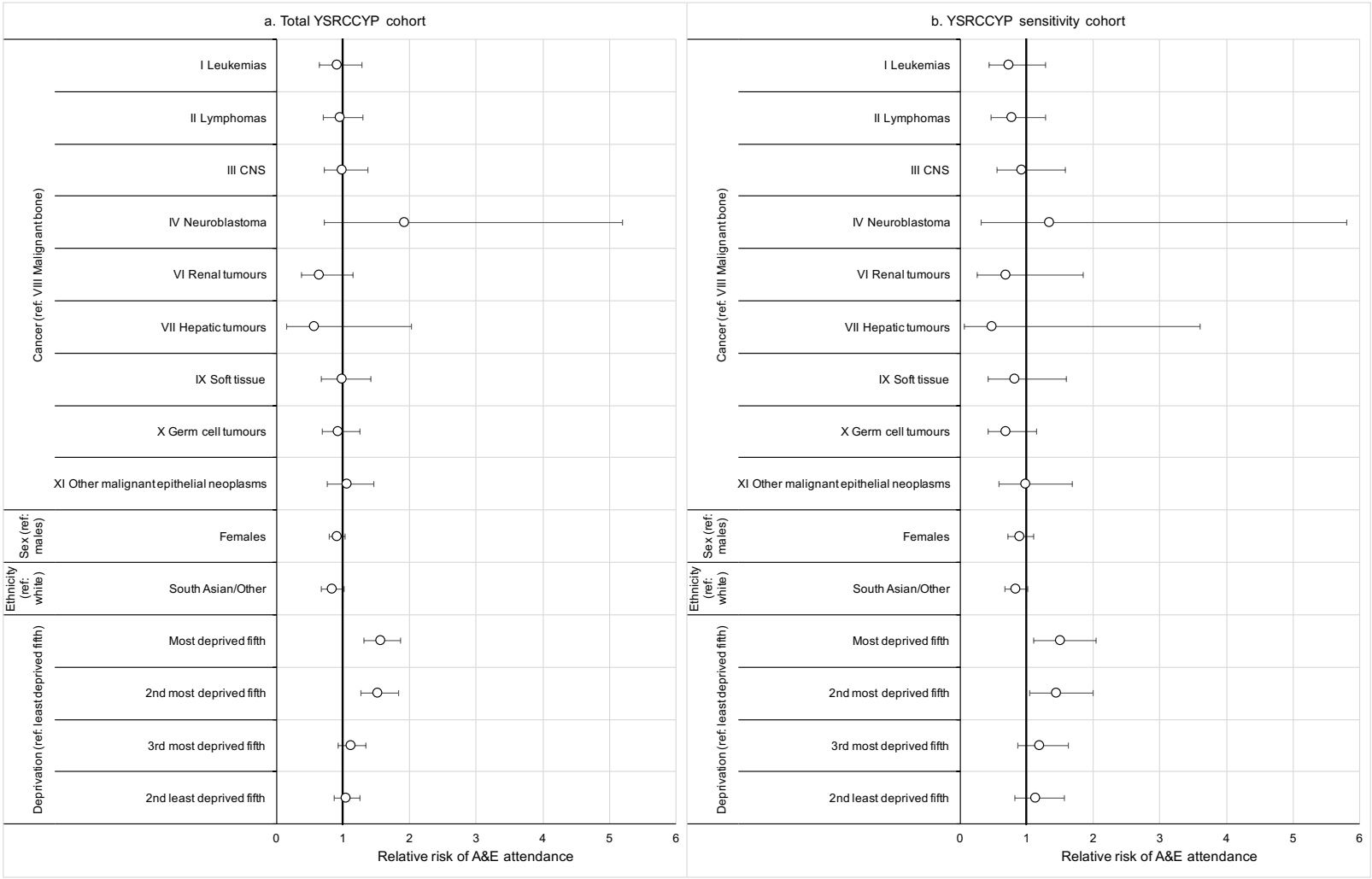


Figure 6.39: Relative risk of accident and emergency (A&E) attendance from mixed effects Poisson model with 95% confidence intervals by cancer type – late cancer onset (a.) and equivalent sensitivity cohort (b.).

6.3.5.6 Accident and emergency (A&E) attendance by mental health admission.

Of the 3,034 individuals in the YSRCCYP cohort with an A&E admission, 373 (12.3%) had a mental health admission before any A&E admission. As with the outpatient and inpatient datasets, there was a higher percentage of individuals with a mental health admission in the late cancer onset group (n=219; 14.5% of the late cancer onset total) compared with early cancer onset (n=154; 10.1% of the early cancer onset total). There was also a higher number of individuals with a mental health admission in the most deprived group (n=119; 15% of the most deprived fifth total) compared with the least deprived fifth (n=46; 9.4% of the least deprived fifth total) (Table 6.21).

Table 6.21: Number of individuals with a mental health admission any time before an accident and emergency (A&E) attendance by socio-demographic groups.

		Total individuals with a mental health admission before an A&E attendance			Total individuals with an A&E attendance
		N	% of group	% of total	
Age at cancer diagnosis	0 to 14 years (early onset)	154	10.1	5.1	1,521
	15 to 29 years (late onset)	219	14.5	7.2	1,513
Sex	Males	202	11.2	6.7	1,802
	Females	171	13.9	5.6	1,232
Ethnicity	White	292	12.2	9.6	2,386
	South Asian/Other	22	9.6	0.7	228
Deprivation	Least deprived fifth	46	9.4	1.5	489
	2nd least deprived fifth	59	10.2	1.9	580
	3rd most deprived fifth	62	12.0	2.0	515
	2nd most deprived fifth	76	13.7	2.5	555
	Most deprived fifth	119	15.0	3.9	795
Total		373	12.3	12.3	3,034

Individuals diagnosed with soft tissue tumours (n=27; 17.4%), CNS neoplasms (n=77; 15.8%) and other malignant epithelial neoplasms (n=30; 14.6%) had the highest percentage of individuals with a mental health admission before an A&E

admission. As with the inpatient data, the lowest percentages were found in retinoblastoma (n=4; 5.7%) and neuroblastoma (n=5; 7.2%) (Table 6.22).

Table 6.22: Number of individuals with a mental health admission any time before an accident and emergency (A&E) attendance by cancer type.

	Total individuals with a mental health admission before an A&E attendance			Total individuals with an A&E attendance
	N	% of group	% of total	
I Leukaemias	58	9.6	1.9	602
II Lymphomas	79	12.3	2.6	642
III CNS	77	15.8	2.5	488
IV Neuroblastoma	5	7.2	0.2	69
V Retinoblastoma	4	5.7	0.1	70
VI Renal tumours	12	9.6	0.4	125
VIII Malignant bone	13	11.8	0.4	110
IX Soft tissue	27	17.4	0.9	155
X Germ cell tumours	67	12.2	2.2	547
XI Other malignant epithelial neoplasms	30	14.6	1.0	205
Total	373	12.3	12.3	3,034

Multi-level logistic regression modelling for the overall cohort found that the odds of an A&E admission with a previous mental health admission was significantly higher than for individuals with no previous mental health admission by four-fold (4.64; 95% CI 1 to 21.55) (Figure 6.40).

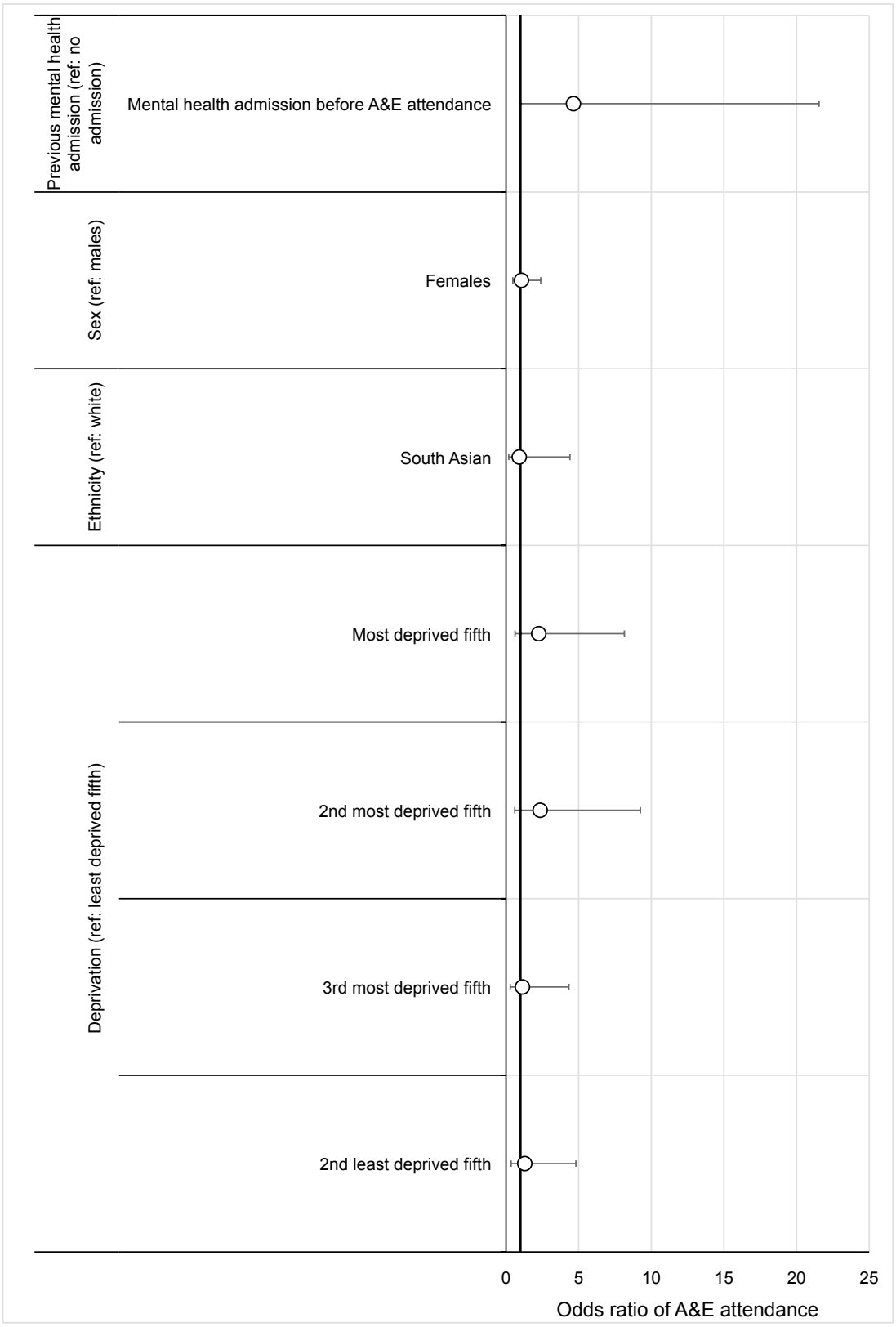


Figure 6.40: Odds ratio of accident and emergency (A&E) attendance from mixed effects logistic regression model with 95% confidence intervals by previous mental health admission.

6.3.5.7 Accident and emergency (A&E) attendance and outpatient appointment status.

In total, 1,733 individuals (39.2%) had an A&E attendance within 90 days of an outpatient appointment. The percentage of individuals with early cancer onset (n=933; 42.8%) was higher than in late cancer onset (n=800; 35.7%). Females (n=808; 43.3%) and South Asian/Other ethnicity (n=159; 42.6%) had a higher percentage of individuals with an A&E attendance 90 days within an outpatient appointment compared with males (n=925; 36.1%) and white ethnicity (n=1,370; 39%). Percentages increased by deprivation group, with the highest percentage in the most deprived fifth at 43.9% (n=468) (Table 6.23).

Table 6.23: Number of individuals with an accident and emergency (A&E) attendance within 90 days of an outpatient appointment by socio-demographic groups.

		Total individuals with an A&E attendance within 90 days of an outpatient appointment			Total individuals with an outpatient appointment
		N	% of group	% of total	
Age at cancer diagnosis	0 to 14 years (early onset)	933	42.8	21.1	2,182
	15 to 29 years (late onset)	800	35.7	18.1	2,242
Sex	Males	925	36.1	20.9	2,563
	Females	808	43.4	18.3	1,861
Ethnicity	White	1,370	39.0	31.0	3,509
	South Asian/Other	159	42.6	3.6	373
Deprivation	Least deprived fifth	275	35.6	6.2	773
	2nd least deprived fifth	300	34.8	6.8	861
	3rd most deprived fifth	293	37.8	6.6	776
	2nd most deprived fifth	332	43.3	7.5	766
	Most deprived fifth	468	43.9	10.6	1,067
Total		1,733	39.2	39.2	4,424

Individuals diagnosed with hepatic tumours (n=11; 47.8%), CNS neoplasms (n=320; 46.7%) and neuroblastoma (n=47; 45.2%) had the highest percentage of individuals with an A&E admission within 90 days of an outpatient appointment. The lowest percentages were found in germ cell tumours (n=220; 29.3%), lymphomas (n=341; 35.6%) and soft tissue tumours (n=88; 37.3%) (Table 6.24).

Table 6.24: Total individuals with an accidence and emergency (A&E) attendance within 90 days of an outpatient appointment by cancer type.

	Total individuals with an A&E attendance within 90 days of an outpatient appointment			Total individuals with an outpatient appointment
	N	% of group	% of total	
I Leukaemias	387	42.6	8.7	908
II Lymphomas	341	35.6	7.7	957
III CNS	320	46.7	7.2	685
IV Neuroblastoma	47	45.2	1.1	104
V Retinoblastoma	40	41.7	0.9	96
VI Renal tumours	71	39.4	1.6	180
VII Hepatic tumours	11	47.8	0.2	23
VIII Malignant bone	74	45.1	1.7	164
IX Soft tissue	88	37.3	2.0	236
X Germ cell tumours	220	29.3	5.0	752
XI Other malignant epithelial neoplasms	130	41.5	2.9	313
Total	1,733	39.2	39.2	4,424

There were 9,480 (10.6%) outpatient appointments where an A&E attendance occurred within 90 days. Of these 9,480 outpatient appointments, 11% (n=1,046) had a DNA status (Table 6.25). This is a similar percentage to the outpatient appointments with no A&E admissions within 90 days at 10.5% (n=8,434).

The mixed effects logistic regression models found no significant difference in odds of A&E attendance within 90 days of an outpatient appointment between attended or DNA appointments (Figure 6.41).

Table 6.25: Number of outpatient appointments and accident and emergency (A&E) attendances by socio-demographic groups and cancer type.

		Total outpatient appointments								Total
		No A&E attendances				A&E attendance within 90 days after an outpatient appointment				
		Did not attend		Attended		Did not attend		Attended		
		N	%	N	%	N	%	N	%	
Age at cancer onset	0 to 14 years (early onset)	4,364	8.6	40,833	80.9	582	1.2	4,636	9.2	50,470
	15 to 29 years (late onset)	4,070	10.4	31,271	80.1	464	1.2	3,216	8.2	39,059
Sex	Males	4,588	10.6	34,523	79.5	546	1.3	3,743	8.6	43,441
	Females	3,846	8.3	37,581	81.5	500	1.1	4,109	8.9	46,088
Ethnicity	White	6,580	9.4	56,753	80.9	819	1.2	5,972	8.5	70,186
	South Asian/Other	788	11.7	5,161	76.5	93	1.4	704	10.4	6,749
Deprivation	Least deprived fifth	1,094	7.1	12,956	84.2	109	0.7	1,225	8.0	15,394
	2nd least deprived fifth	1,250	7.4	14,130	83.9	131	0.8	1,321	7.8	16,843
	3rd most deprived fifth	1,436	9.6	12,105	81.0	154	1.0	1,220	8.2	14,942
	2nd most deprived fifth	1,644	9.8	13,131	78.4	228	1.4	1,719	10.3	16,749
	Most deprived fifth	2,653	12.1	16,830	76.6	387	1.8	2,076	9.5	21,960
Cancer type	I Leukaemias	2,022	9.9	16,630	81.1	189	0.9	1641	8.0	20,497
	II Lymphomas	1,783	10.5	13,724	80.4	232	1.4	1305	7.6	17,060
	III CNS	1,238	6.6	15,224	80.8	176	0.9	2193	11.6	18,851
	IV Neuroblastoma	241	9.9	2,036	83.7	25	1.0	129	5.3	2,433
	V Retinoblastoma	242	12.3	1,602	81.2	12	0.6	110	5.6	1,973
	VI Renal tumours	360	9.8	2,873	78.4	40	1.1	383	10.5	3,665
	VII Hepatic tumours	17	4.3	330	83.5	5	1.3	43	10.9	395
	VIII Malignant bone	296	7.9	3,083	82.8	48	1.3	295	7.9	3,724
	IX Soft tissue	409	8.4	4,002	82.1	55	1.1	404	8.3	4,873
	X Germ cell tumours	1,069	12.0	6,979	78.5	181	2.0	646	7.3	8,887
	XI Other malignant epithelial neoplasms	741	10.9	5,370	78.9	80	1.2	606	8.9	6,804
Total		8,434	9.4	72,104	80.5	1,046	1.2	7,852	8.8	89,529

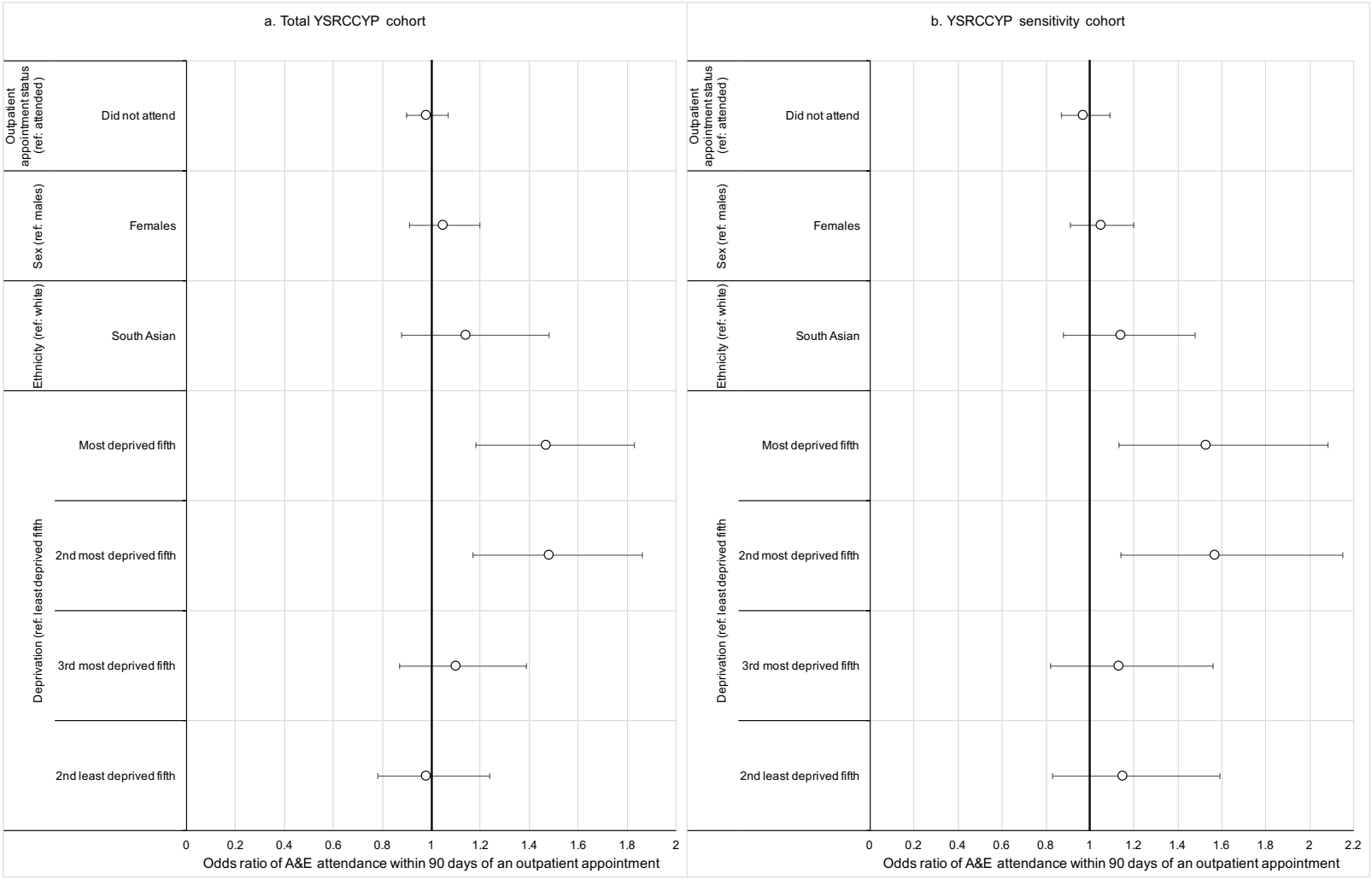


Figure 6.41: Odds ratio of accident and emergency (A&E) attendance within 90 days of an outpatient appointment from mixed effects logistic regression model with 95% confidence intervals (a.) and equivalent sensitivity cohort (b.).

6.4 Summary of results.

Mental health admission had the lowest incidence rates of all outcomes from the HES and MHMDS analysis. Most of these admissions were diagnosed after the transitional care period and/or at least 5 years after initial cancer diagnosis. Risk of a mental health admission was higher for males and individuals diagnosed with leukaemias, lymphomas, CNS neoplasms and germ cell tumours. These cancer types also had the highest total of outpatient appointments and inpatient admissions with a mental health treatment specialty. Individuals with a mental health admission had a significantly higher odds of a DNA outpatient appointment in late cancer onset and also had an increased risk of an A&E attendance compared with individuals with no record of a mental health admission. However, there was no significant difference in inpatient admission between individuals with and without a previous mental health admission. No significant differences were found between ethnicity categories, nor between deprivation fifths.

Although the DNA rate of outpatient appointments was relatively low at 10.3%, over 60% of individuals had at least one missed appointment. The incidence of a DNA appointment was significantly higher in late cancer onset compared with early cancer onset. In early cancer onset, during the transitional care period, the odds of a DNA appointment compared with the 10 to 14-year age group was significantly higher in the 20 to 24-year age group than in the 15 to 19-year age group. However, the odds were not significantly different from the age groups after the transitional care period. This was also found in late cancer onset, where the odds of a DNA appointment compared with the 40 and over group were not significantly different between the age groups during the transitional care period and age groups after the transitional care period.

On average, around 4 appointments were missed out of 25 appointments per individual. Females had a higher incidence of DNA appointments compared with males, but their odds of a DNA appointment were significantly lower compared with males. There was no significant difference in DNA appointments between ethnicity categories or cancer types. However, there was some evidence for significantly higher odds for the most deprived fifth compared with the least deprived fifth.

Outpatient appointments with a mental health treatment specialty, particularly in late cancer onset, had a higher odds of a DNA appointment compared with oncology appointments and also had the highest odds ratio of all other treatment specialities. Appointments with a treatment specialty of Maternity/Obstetrics/Gynaecology had the lowest odds of a DNA appointment

compared with oncology. DNA appointments did not increase the risk of an A&E attendance. However, it was found that a DNA appointment actually significantly decreased the odds of a CIPS by around 50%.

Inpatient admissions had the highest incidence rates for all outcomes. There were no significant differences in CIPS incidence rates between early and late cancer onset. Incidence was higher in older ages and risk of CIPS was higher for older age groups, although this was disputed by the sensitivity cohort which showed an opposite trend. As with DNA outpatient incidence, females also had a higher incidence for CIPS compared with males. However, where females were found to have significantly lower odds of a DNA outpatient appointment compared with males, females had a significantly higher risk of a CIPS compared with males. Although the South Asian/Other category also had higher CIPS incidence, there was significant difference in risk of a CIPS in the South Asian/Other group compared with white ethnicity. There was some evidence of significantly higher risk of CIPS in the most deprived fifth compared with the least deprived fifth.

No primary diagnoses had a significantly higher risk of CIPS compared with oncology. In late cancer onset, mental health behaviour had the highest risk of CIPS than all other diagnoses compared with oncology. However, in early onset mental health behaviour had one of the lowest risks of CIPS.

The incidence rates for A&E were less than the incidence rates for CIPS. The incidence and risk of an A&E attendance was higher in older age groups. As with the outpatient and inpatient data, there were no significant differences in risk of A&E attendance between ethnicity groups and risk of an A&E attendance was higher in the most deprived fifth compared with the least deprived fifth. There were no significant differences in risk of A&E attendance by cancer type.

6.5 Overall summary analysis compared with previous studies.

The rate of CIPS in the YSRCCYP was over twice that of the rate found in a study in Amsterdam for 5-year survivors diagnosed with cancer before 18 years, reaching 172 hospitalisations per 1,000 person-years (205). However, this was only a single-centre study of 1,564 individuals, covering an 11-year period between 1995 to 2006. The YSRCCYP covered a 20-year period between 1997 to 2017 with 7,238 individuals, including late onset diagnoses. In the multi-centre Cancer in Childhood Survivor Study (CCSS), the rate was also found to be half the rate of the YSRCCYP at 142.1 per 1,000 person-years with 13-years follow-up between 1992 and 2005 (204). This may be explained by the use of

survey data in the CCSS to determine hospitalisation rate, which may not have produced accurate estimates due to reliance on recall memory compared with using routine data as used in this study.

6.6 Health outcomes by attained age groups before, during and after the transitional care period.

The relative risk of CIPS and A&E attendance in the YSRCCYP at the beginning of the transitional care period in the 15 to 19-year age group was significantly higher compared with the 10 to 14-year age group. This suggested an increase in negative health outcomes begins during the transitional care period. This increasing trend in relative risk continued after the transitional care period, with the highest relative risk in the oldest age group. The sensitivity analysis showed a decreasing trend in relative risk with increasing age groups, although this could be due to fewer individuals in the cohort at older age groups.

This increase in hospitalisations with older ages was also found by Wijlaars and colleagues, who analysed all hospital inpatient admissions and A&E attendances in England over 3 years between individuals with and without an LTC (including non-cancer conditions). They found a significant increase in admission rates after transition (defined as ages 19 to 24 years) at a higher rate for those with an LTC compared with the general population. They also found an increase in hospitalisations after transition for mental health admissions for both LTC and non-LTC groups (285). In this study, most first known mental health admissions occurred during the transitional care period (n=318; 53%) and after cancer diagnosis (n=508; 84.4%). However, there were no significant differences in relative risk of first known mental health admission for any age group compared with the 10 to 14-year age group overall, suggesting that there was no significant increase in risk during the transitional care period.

The relative risk of an outpatient appointment with a DNA status was significantly higher during and after the transitional care period compared with before. The trend in relative risk of an outpatient appointment with a DNA status increased significantly from 15 to 19-years to the 20 to 24-year age group. However, the relative risk in all older ages remained similar to the 20 to 24-year age group, so outpatient appointment attendance was no worse during the transitional care period compared with after the transitional care period. This suggests that older adults were similarly less compliant at outpatient appointment attendance than younger adults.

6.7 Health outcomes by onset before and during the transitional care period.

The incidence rate for an A&E attendance following a cancer diagnosis was significantly higher in late onset compared with early onset. This may be due to the late cancer onset group including more individuals followed up at older ages, where a higher proportion of A&E attendances occur. In 2017-18, 10% of all A&E attendances in England occurred in 5 to 14-year olds, whilst nearly 30% occurred in 15 to 34-year olds (286). There were no significant differences in relative risk for an A&E attendance between any cancer types in either onset group, suggesting that initial cancer diagnosis was not associated with A&E attendance during follow-up.

The incidence rates for outpatient appointment with a DNA status was also significantly higher for late onset compared with early onset. When assessing attendance at outpatient appointments for mental health in comparison with oncology appointments, the late onset group had a higher odds ratio of a DNA status compared with early onset. Significantly fewer outpatient appointments with a DNA status were found for those diagnosed with CNS neoplasms compared with the reference cancer group in early cancer onset, but not for late cancer onset.

The incidence rate for first mental health admissions was also significantly higher in late cancer onset compared with early cancer onset. Kazak and colleagues found that those diagnosed during adolescence had poorer psychosocial outcomes compared with peers and that treatment severity was an important risk factor due to associations with cancer type and impact on quality of life (247). In both onset groups, individuals diagnosed with leukaemias, lymphomas and CNS neoplasms (and germ cell tumours in late cancer onset) all had significantly higher risk of a mental health admission when compared with the reference cancer types. These cancer types were the most frequently diagnosed in both onset groups. As in the overall cohort, there were no significant differences in relative risk between age groups for first mental health admission in early cancer onset. However, for the late cancer onset group, significantly higher relative risk of first mental health admission was found for those aged 20 to 34 compared with the 40 and over group, with a peak relative risk in those aged 25 to 29-years. As with the YRDCYP, this suggests that those diagnosed during the transitional care period may need increased mental health support. The YSRCCYP found that individuals in the latter stages of the transitional care period (25 to 29 years) in particular required

increased support. This age group was often overlooked in assessing transitional issues.

Despite higher incidence rates in late cancer onset for DNA outpatient appointments, A&E attendance and first mental health admission, no significant difference in incidence rate for CIPS between the onset groups was found. An explanation for this may be due to a higher mean number of CIPS per individual in the early onset group. A higher mean number of total outpatient appointments per individual was also found in the early onset group. As more outpatient appointments were attended at younger ages, there could be more opportunity for a referral for an inpatient admission. The possible link between DNA outpatient appointments and inpatient referral has not been explored in previous research, so future examination of this association is needed.

Almost a third of CIPS had a primary diagnosis code for neoplasms and around a fifth had a treatment specialty of oncology. As this analysis only included data from at least 5 years after diagnosis of initial cancer, it was assumed that treatment for the first cancer was completed so it is likely that some of these admissions are related to a subsequent cancer diagnosis. Previous research has shown a 47% increased risk of developing subsequent cancer (63). For all cancer types, apart from hepatic tumours, neoplasm was the most frequent primary diagnosis. Oncology was the most frequent treatment specialty for CIPS for leukaemias, lymphomas, CNS neoplasms, malignant bone tumours, soft tissue tumours and other malignant epithelia neoplasms. There was a level of uncertainty as to whether these CIPS refer to a subsequent cancer and if so, what types of cancer have occurred. Validation against the YSRCCYP for these instances was not possible as data were only available for individuals with a second cancer diagnosis under the age of 30, so would not capture all cases. In the British Childhood Cancer Survivor Study (BCCSS), it was found that the most frequent secondary cancers were CNS neoplasms, non-melanoma skin cancer, digestive, genitourinary, breast and bone cancers (70).

6.8 Health outcomes by socio-demographic groups and cancer type.

Females had a significantly higher two-fold relative risk of CIPS compared with males. Females were more likely to attend outpatient appointments, so had more opportunity to be referred for an inpatient admission. Relative risk of A&E attendance for both early and late cancer onset showed no significant difference between sexes.

The higher proportion of deaths from suicide for males in the YRDCYP T1D analysis suggested issues surrounding mental health in males. This was also shown in the YSRCCYP cohort where mental health admission was significantly higher in males compared with females. Males also had worse attendance at outpatient appointments compared with females, with the highest risk of a DNA status in the mental health treatment specialty. This was similar to a report on outpatient appointments in Scotland (including non-cancer patients), where there were higher DNA outpatient appointments for males and also for general psychiatry. However, it was deprivation rather than sex that was a significant predictor for non-attendance to the psychiatry appointments (287). In this study, there was no significant difference between deprivation groups for mental health admissions. There was a significantly higher odds ratio of a DNA outpatient appointment in the most deprived fifth compared with the least deprived fifth and A&E attendances were also significantly higher in the two most deprived groups.

For ethnicity, there were no significant differences between the South Asian/Other group compared with white ethnicity for CIPS, outpatient appointment DNA status and A&E attendance. However, there was a significantly lower risk of a mental health admission for the South Asian/Other group compared with white ethnicity. As there were smaller numbers for mental health admissions and possible classification issues with Onomap, this significant result for mental health admissions may need to be considered with caution.

6.9 Health outcomes by hospital outpatient appointment attendance.

The total percentage of non-attended outpatient appointments (10.3%) in the YSRCCYP was similar to appointment outpatient attendance in the general population of Scotland at 10% (287). Compared with England and Wales, 13% of all individuals with a DNA outpatient appointment had an unplanned A&E attendance within 90 days. This compared to 8.4% of individuals who attended their outpatient appointment (288). In the YSRCCYP, 39.2% of all outpatient appointments were followed by an A&E attendance within 90 days. Of these outpatient appointments, 11% of those with a DNA status had an A&E attendance within 90 days, compared with 9.8% of those with an attended status. Therefore, the YSRCCYP had similar percentages of A&E attendance 90 days after an outpatient appointment compared with the general population.

There was no significant difference in relative risk for an A&E attendance within 90 days between attended and DNA outpatient appointments.

The significantly lower relative risk of a CIPS 90 days after an outpatient appointment with a DNA status may lead to the assumption that non-attendance to outpatient appointments has no detrimental effects to health outcomes. There was also no significant difference in relative risk of an A&E attendance 90 days after an outpatient appointment between DNA and attended status. This supported the view that non-attendance does not necessarily mean non-adherence and that appointments may be missed as they are less likely to be needed (115). However, non-attendance at an outpatient appointment may mean that there was less opportunity for a referral for an inpatient admission. The consequence of this may be that a higher risk of A&E attendance in the longer term. Previous research into the association between outpatient, inpatient and A&E datasets is lacking and requires further study.

6.10 Health outcomes by mental health history.

According to the latest psychiatric morbidity survey of England, it was estimated that around 13.1% of adults were receiving mental health treatment (289). This was higher than that found in the YSRCCYP, where 8.3% received a mental health admission either before, during or after initial cancer treatment, suggesting that mental health treatment is higher in the general population. However, the MHMDS only captured secondary care services and did not include GP services, so it was likely that analysis on mental health for the YSRCCYP was underestimated. Previous studies have shown that physical illness increases mental health issues. Bagur and colleagues found that psychiatric disorders were significantly higher in childhood cancer survivors compared with the general population and as much as 56.2% of survivors having at least one psychiatric disorder (243).

In the YSRCCYP, a history of a mental health admission was shown to increase the risk of having an outpatient appointment with a DNA status and an increased risk of attending A&E. This suggested that mental health issues are a barrier to outpatient appointment attendance and a risk factor for A&E attendance. As most first known mental health admissions occurred after 5 years since initial cancer diagnosis, this suggested that support for mental health was important not only during cancer treatment but especially during follow-up. In a UK focus group, Brown and colleagues (2016) found that childhood cancer survivors talked about how their cancer treatment not only had long-term consequences on physical health but also consequences on social

relationships and emotional perceptions of the self (290). Other surveys and qualitative studies have reported similar issues continuing into adulthood. It has also been noted that poor physical health is associated with higher rates of unemployment, which in turn leads to a lower quality of life and increases mental health issues (291) (292). In this study, although there was an increased incidence rate of mental health admission in the most deprived groups, there were no significant differences in relative risk of mental health admissions between any of the deprivation fifths compared with the least deprived fifth, suggesting that deprivation was not a predictor for a mental health admission. However, it could not be established with these data whether everyone who needed mental health services had access to care. For example, the most deprived groups may have been in more need of mental health services, but whether these groups had the same opportunities to access these services compared with individuals in the least deprived groups was not known.

6.11 Chapter summary.

Analysis of HES data for the YSRCCYP showed that the risk of negative health outcomes (CIPS, A&E attendance and DNA outpatient appointments) significantly increased during the transitional care period compared with before. However, this risk continues into older adulthood, so this increase was not specific to the transitional care period. Mental health admissions found no significant differences between before and during the transitional care period. However, incidence of mental health admissions, as well A&E attendances and DNA outpatient appointments were significantly higher in late cancer onset compared with early onset.

As with T1D health outcomes, there were significant differences in CYA cancer health outcomes between sex groups. The risk of a mental health admission and a DNA outpatient appointment was significantly higher in males compared with females, whilst risk of CIPS was significantly higher in females compared with males. No significant differences were found between sex groups for A&E attendances.

Mental health attendance was significantly higher in white ethnicity compared with South Asian ethnicity. Unlike with T1D mortality, the most deprived groups had significantly higher A&E attendances and DNA outpatient appointments.

Chapter 7 Discussion

Despite clinical recognition that the transitional care period conceptualises more than the transfer between paediatric to adult services, current quantitative research on this topic tends to only focus on analysis for attended appointments before and after transfer, partly due to the lack of available long-term data collected for the purpose of studying the effects of transition. The justification for specialist transition services is based on qualitative research, with no empirical measure of the need for these services based on assessment of long-term health outcomes. This study used routine population-based registry datasets collected over a 35-year period to overcome this paucity of quantitative research. These datasets were linked with mortality and hospital admissions data to examine the health outcomes related to the transitional care period in both T1D and CYA cancer. Analysis of the YRDCYP cohort linked with ONS death certification data (Chapter 4) found that most deaths in individuals with T1D occurred during the transitional care period, with deaths due to DKA at 15 to 19 years of age exceeding the mortality rate for the overall cohort. Mortality was also higher in the late T1D onset group compared with early T1D onset. CSII therapy in the LCYPDS was shown to be effective in reducing HbA1c levels during the transitional care period for up to 4 years after the start of treatment, although females sustained HbA1c improvements for a shorter time period and discontinued CSII therapy more than males (Chapter 5). In the YSRCCYP cohort linked with HES and MHMDS data (Chapter 6), the likelihood of a mental health admission, a DNA outpatient appointment, A&E attendance and CIPS were significantly higher during the transitional care period compared with before in CYA cancer. As with T1D mortality, the risk of negative health outcomes in the YSRCCYP was higher in late onset compared with early onset.

The results for each cohort were discussed overall (sections 4.5, 5.5 and 6.5) and then in relation to attained age (sections 4.6, 5.6 and 6.6), age at onset (sections 4.7 and 6.7) and socio-demographic characteristics (sections 4.8, 5.7 and 6.8). For the YSRCCYP cohort, results by outpatient attendance (section 6.9) and mental health admission (section 6.10) were discussed.

This chapter includes a discussion of the results in the context of the study hypothesis (section 7.1), the major implications of this study (section 7.2), the strengths and weaknesses (section 7.3), future work (section 7.4) and conclusion (section 7.5).

7.1 Addressing the study hypothesis.

This study hypothesised that there would be an increase in negative health outcomes during the transitional care period, compared with before and after for both T1D and CYA cancer. The results of analysis from both the YRDCYP and YRSSCYP cohorts demonstrated that rates of negative health outcomes could be compared before, during and after the transitional care period, with some evidence of an increase in negative health outcomes during the transitional care period, although this was not found to be consistent in all age groups. In the YRDCYP, DKA mortality was highest in the 15 to 19-year age group but no significant difference was found compared with the overall mortality rate for ages 20 to 29 years. Problems with DKA for under 19-year olds was also shown in the LCYPDS where there was a significantly higher hospitalisation rate for DKA in the first year of CSII, although there was insufficient data to compare health outcomes before, during and after the transitional care period for the LCYPDS cohort.

This increase in DKA mortality risk in the younger ages of the transitional care period was not observed for other causes of death in the YRDCYP. For overall mortality in the YRDCYP, there was an increasing trend in SMRs from the 15 to 19-year age group, peaking at 25 to 29-year age group, before decreasing at older ages. However, there were no significant differences found between during the transitional care period and afterwards. These trends were also shown in the YRSSCYP cohort, where there were significant increases in negative health outcomes beginning during the transitional care period compared with before, but there were no significant differences found compared with older age groups. These routine data indicated that the transitional care period marked the start of an increase in negative health outcomes across both T1D and CYA cancers. However, this does not provide definitive evidence for the need of specialist transition services across all diseases. It could not be determined in the data whether a reduction in negative health outcomes during the transitional care period could reduce the risk of negative health outcomes in older ages. The association between the risk of negative outcomes during the transitional care period and afterwards warrants further investigation.

This study analysed socio-demographic groups to determine whether there is a need for further targeted interventions for specific groups of individuals. The analysis of the YRDCYP found a significantly lower risk of death for females compared with males for all causes apart from T1D acute complications, where there were no significant differences in risk found between males and females. This would suggest targeted interventions would be beneficial for males. However, in the LCYPDS, females were found to have higher CSII

discontinuation rates and less improvement in HbA1c with CSII compared with males. The higher percentage of females initiating CSII treatment also indicated a possible increase of issues surrounding HbA1c control with MDIs compared with males. This demonstrated that assessing a single source of routine data for one type of negative health outcome cannot capture the complexity of the need for targeted interventions for specific socio-demographic groups. This was also shown with the YSRCCYP cohort where males were at higher risk of a mental health admission and a DNA outpatient appointment compared with females, whereas females had a significantly higher risk of a CIPS.

Analysis by age at LTC onset also found some notable differences between groups for negative health outcomes in both T1D and CYA cancer. The late onset groups were shown to have an increased risk of T1D mortality and higher incidence of DNA outpatient appointments, A&E attendance and mental health admission. This could be due to the inclusion of older age groups for individuals diagnosed with late LTC onset who were more likely to develop negative health outcomes. Another reason could be due to the amount of experience and preparation in managing an LTC in adulthood. Investigating individual experiences is difficult to quantify, so using routine data in isolation can be limited. Although qualitative data are subjective and usually only include a small sample of the population, they are still valuable in providing insight and context in explaining certain trends found using quantitative methods.

For the YSRCCYP cohort, analysis of outpatient appointments found a significantly lower risk of a CIPS 90 days after a DNA outpatient appointment. This could indicate that non-attendance to outpatient appointments has no detrimental effect on health outcomes, supporting the view that non-attendance does not necessarily mean non-adherence in CYA cancer survivors. However, non-attendance at an outpatient appointment may mean that there was less opportunity for a referral for an inpatient admission and may lead to a higher risk of an A&E in the longer term or premature death. Using CIPS as a proxy measure for complications would therefore be questionable as this dataset would not be able to capture complications where there was no inpatient admission. To investigate this further, as with age at onset, qualitative research may provide some insight as to why there is a decreased risk of CIPS with DNA appointments, alongside further analysis of outpatient, inpatient and A&E datasets.

Due to the heterogeneity of cancer, analysis was conducted by cancer type in the YRSCCYP. Analysis by treatment specialty and diagnosis codes was also completed to determine any differences between complication types for outpatient and inpatient data. This produced a high volume of results with no

significant associations. Inclusion of all of these results may not have been relevant for this thesis. However, they may provide some insight for future researchers interested in performing similar analysis for comparison.

The analyses presented in this thesis demonstrated that routine datasets can be used to examine whether negative health outcomes increase during the transitional care period and whether certain groups of individuals were more at risk of negative health outcomes. However, this thesis also highlights limitations to using analysis of datasets in providing evidence for specialist transition services. Using multiple datasets revealed the underlying complexity in associations in risk of negative health outcomes for certain groups which would not have been found by assessing only one dataset for an LTC. There were some common significant associations found in both T1D and CYA cancer indicating that there are similarities surrounding transitional issues across diseases, but disease-specific trends also imply the need to assess LTCs separately.

7.2 Clinical implications of this study.

A main concern was the increased risk of mental health issues in males in the YRDCYP and YSRCCYP cohorts, particularly during the transitional care period. For T1D, the increased mortality rate in the 15 to 19-year age group suggests that management of T1D was poor during the transitional care period. This was reflected in the latest National Diabetes Audit (NDA) for 2016-17 which showed only 33.7% of all individuals with T1D in England and Wales received 8 of the 9 recommended annual care processes and only 19% reach treatment targets for HbA1c, blood pressure and cholesterol. These percentages for care process completion and treatment target achievement were worse at younger ages (190). During adolescence, maintaining tight metabolic control can be difficult, not only because of increased insulin resistance during puberty but also due to psychosocial issues created by changing life stages coinciding with the period of transition between child to adult orientated services (293,294). In Gibb and colleague's (2016) study on DKA hospitalisations in Edinburgh, 13.1% of those with recurrent DKA (5 or more presentations of DKA) had an inpatient admission for psychiatric care compared with 4.3% with a single DKA admission (270). This suggests that there may be a relationship between mental health and acute complications in T1D. However, the direction of the association (i.e. whether it is mental health which affects acute complications or whether acute complications affects mental health) has not been explored in previous research.

In both the YRDCYP and YSRCCYP, there were differences in mental health issues between the onset groups. For the YRDCYP, there was a higher risk of death from mental health disorders and suicide in late T1D onset compared with early T1D onset. In the YSRCCYP, the incidence rate of a mental health admission was significantly higher in late cancer onset compared with early cancer onset. This suggested that individuals diagnosed with a chronic illness within the transitional care period needed greater attention for mental health support. Despite a greater specialised focus in cancer treatment being in place for young adults compared with T1D as described in section 1.2, of all individuals of late cancer onset with a mental health admission, nearly a quarter had their first known mental health admission within the first 5 years since their initial cancer diagnosis. There was a significantly higher relative risk of first mental health admission found for those aged 20 to 34 years compared with the 40 and over group, with a peak relative risk in the 25 to 29-year age group. This showed the importance of targeting mental health support for those in the older age groups in the transitional care period. The current NICE clinical guidelines have clear definitions of when transitional care should begin (20), but there is no recommendation for when transitional care ends. This study showed that the older age groups of the transitional care period should not be overlooked, and this should be reflected in clinical recommendations and guidelines.

In this study, the analysis of CIPS was intended to be used as a proxy measure for long-term health outcomes. As there was a significantly lower relative risk of a CIPS 90 days after an outpatient appointment with a DNA status, this may lead to the assumption that non-attendance to outpatient appointments had no detrimental effects on health outcomes. This supports the view that non-attendance does not necessarily mean non-adherence and that appointments may be missed as they are less likely to be needed (115). However, non-attendance at an outpatient appointment meant that there was less opportunity for a referral for an inpatient admission. Therefore, there may have been an underestimation of negative health outcomes when using inpatient data in isolation as a proxy measure. Although there were no significant association between outpatient attendance status and A&E attendance, the multi-level modelling in this study only considered A&E attendances within 90 days. The consequence of not being referred for an inpatient admission due to non-attendance at an outpatient appointment may be increased A&E attendances in the longer term or premature death. If this is the case, this would imply that preventing non-attendance at outpatient appointments is vital to avoid long-term negative health outcomes. Therefore, more concerted effort is needed to develop strategies to improve attendance rates.

7.3 Strength and weaknesses of this study.

This study used registry data, covering the population of Yorkshire over a period of 35 years. It thus provides a complete population-level analysis comprising long-term follow-up information. As these were routine datasets, these were cost-effective and readily available for analysis. However, some data were missing, incomplete or incorrect. This limited some components of the analysis and caused some difficultly when linking the cohort data to mortality and HES datasets. The linkage of the YSRCCYP cohort to the individuals HES datasets and the second linkage between the HES datasets was time consuming due to the complexity of cleaning rules required. However, the final datasets could be used to analyse a range of research questions in addition to this study. The knowledge gained during the data linkage process can also be standardised for other HES datasets.

Analysis by ethnicity and deprivation has been infrequently included in previous studies. This is due to poor completion of these data, which is not always mandatory in administrative datasets. In both the YRDCYP and YSRCCYP cohorts, Onomap software was a useful and easily applicable tool to identify ethnicity using full name of individuals. However, despite its good coverage of a large number of ethnic groups and the ability to use different dimensions of identity to derive a classification group (254), there were still a large number of individuals in both cohorts with missing ethnicity after the algorithm was applied (n=1,782 (32%) in the YRDCYP and n=1,633 (22.6%) in the YSRCCYP) . There were also problems with the algorithm in considering marital status for females and the identification of mixed ethnicities. Around 32% of both the YRDCYP and YSRCCYP had incomplete full names. The consequence of this may have led to an underestimation of the South Asian/Other total.

Classification errors may also have occurred for deprivation. Larger populations live within the most deprived YRHA wards, leading to a higher proportion of the cohort classified in the most deprived fifth. The Index of Multiple Deprivation is calculated by Output Areas which are approximately equal in population size, so provides a more equal spread across the five deprivation categories. However, Townsend index was preferred due to its focus on material deprivation. No difference in trends were found in this study when using IMD in comparison to Townsend score.

7.3.1 Yorkshire Register of Diabetes in Children and Young People (YRDCYP) cohort linked to Office for National Statistics (ONS) mortality data.

The underlying cause of death fields on the ONS mortality data were coded from death certification data using ICD-10 codes. Specialist clinician assessment of these codes was vital in producing an accurate analysis of cause-specific mortality as there were many inaccuracies in the coding. For example, deaths originally classified as renal disease with no reference to diabetes were reclassified ICD-10 code E10.2 (T1D with renal complications). According to the specialist clinician, deaths originally coded for ischaemic heart disease (IHD) should have been coded for T1D with IHD. However, there was no ICD-10 code for this cause of death, so these deaths were coded under E10.6 (type 1 diabetes with specified complications). Only 54% of all death certificates mentioned diabetes and 21% specifically mentioned T1D. The absence of T1D recorded on death certificates for individuals with a confirmed diagnosis has been highlighted previously in an Australian registry; around 38% of CVD deaths were underestimated after evaluation from a clinical specialist. However, only codes with underlying cause of death with ‘uncomplicated diabetes’ or ‘diabetes with circulatory complications’ were re-examined (295). A key strength in the analysis of this study included a systematic re-evaluation of all ICD-10 codes.

The lack of clinical data to examine associations between previous health history with mortality limits the analysis of the YRDCYP cohort. Data on HbA1c levels, mental health history, lifestyle and co-morbidity for other diseases would have been useful in informing whether these factors were also contributors to excess mortality, as well as socio-demographic groupings. The NPDA combined with hospital admissions data to assess socio-demographic groups and treatment regimen in rates of acute complications over a 3-year period (126). Combining this with long-term mortality data would be valuable in identifying additional clinical predictors which increase the risk of death.

7.3.2 Leeds Children and Young People’s Diabetes Service (LCYPDS) cohort for continuous subcutaneous insulin infusion (CSII) therapy.

The analysis of HbA1c level pre-, during and after CSII therapy used multi-level modelling to account for the assumption of independent observations which has been rarely performed previously and is a major strength of this study. This was

not considered in other studies where HbA1c levels are examined, meaning that it was difficult to compare these results with previous studies. Also, as this was a centre-specific dataset, care must be taken when generalising these results nationally. The 2016-17 NPDA found that the Yorkshire and the Humber region had the highest percentage of CSII therapy in England and Wales (296). This means that the LCYPDS may represent one of the more proactive services in the country in prescribing CSII therapy and may have more trained staff and resources compared with other services across the country.

Another weakness of this dataset was the unavailability of data for individuals remaining on MDIs. Due to the different stages of insulin resistance in adolescence, the sustainment of HbA1c improvement with CSII therapy for 4 years could correspond to this trend (277). As the LCYPDS dataset was limited to individuals up to aged 19 years, it could not be determined whether HbA1c levels begin to decrease again in young adulthood. These fluctuations in HbA1c levels for those on CSII was similar to that of individuals on MDI therefore it was not clear which of these therapies gave optimum performance.

7.3.3 Yorkshire Specialist Register of Cancer in Children and Young People (YSRCCYP) cohort linked to HES and MHMDS datasets.

Although using HES data to examine health outcomes has been performed in previous studies, no other published studies have linked different HES datasets together to assess a more complete picture of the treatment journey through the secondary care system for a childhood or young adult cancer survivor. However, data for HES were not available from the start of the YSRCCYP diagnostic period, so there may have been missing data for individuals diagnosed before 2002 for at least one of the HES datasets. The sensitivity analysis to assess this level of bias showed opposite trends for age in models for CIPS for early cancer onset and A&E admissions for both early and late cancer onset. An explanation for this may be due to the lower numbers of individuals at older ages in the sensitivity cohorts. All other sensitivity models showed similar trends to analysis for the overall cohort. Therefore, any bias in this cohort appeared to have had minimal effect on the overall results and conclusions of this study.

This study showed the importance of mental health in attending outpatient appointments and preventing A&E attendances. However, the MHMDS dataset was limited as it only included individuals receiving treatment from secondary care services and so there may have been an underestimation of mental health

issues in the YSRCCYP. There were also issues around the quality and accuracy of the MHMDS data. For some individuals with multiple admissions, there were different years recorded for when the first known psychiatric care episode took place, suggesting that this field could often be inaccurately recorded. Some records could be verified on the inpatient dataset, although this only included 10% of the dataset.

7.4 Future work.

Mental health support has been highlighted as an important topic in this study. Linking the MHMDS to the YRDCYP and LCYPDS cohorts along with clinical data such as HbA1c values would provide valuable analysis for the effect of mental health on self-management of T1D. It would also provide additional information on whether mental health is a factor for discontinuing CSII therapy, despite the limitations of the MHMDS dataset. The addition of primary care data would provide greater accuracy in determining the total number of individuals receiving mental health treatment. However, there would still be an underestimation of individuals in need of mental health services without a methodology to identify individuals in need of treatment but who are not known to any services. Data on the type of mental health condition and the type of treatment would further provide important details about whether the type/severity of mental health disorder or treatment used has any effect on physical health outcomes for both T1D and cancer.

The evidence for more mental health issues in late onset compared with early onset in both the T1D and cancer cohorts showed that there is a need to examine the effects of being diagnosed with a chronic illness during the transitional care period. The burden of diagnosis coinciding with multiple life transitions may create more emotional and practical difficulties compared with an individual who has grown up with a chronic illness since childhood. There is a paucity of research on this topic and this is reflected in the lack of separate clinical guidelines or recommendations on this group of individuals. Due to the societal changes of ‘emerging adulthood’ where life transitions are extended over a longer period of time, such as AYAs moving out of the familial home and staying in full-time education at older ages, it may be that the transitional care period will need to include older age groups. This means that future research should pay close attention to these changes, leading to new issues for older age groups.

The purpose of this study was to assess the empirical evidence for the need for specialist transition services. However, it did not evaluate whether current

specialist services are meeting current needs of adolescents and young adults. Whilst previous studies have focused on appointment attendance in these specialist services, few studies have assessed these services on health outcomes. In a future planned research study, data from the LCYPDS will assess whether there are differences between individuals who attended the service and then transferred to adult services with individuals who attended the transition clinics for adolescents and young adults introduced in 2008. Although we would not have the data to assess long-term outcomes, this study would be able to assess whether there has been an improvement since the introduction of the transition clinics for short-term outcomes.

The finding relating to the possible association between missed outpatient appointments and fewer inpatient admissions requires extended examination. Analysis of whether a certain percentage of missed appointments or whether the most recent appointments are missed has any influence on inpatient admissions warrants closer inspection, in addition to how this possible association affects long-term A&E attendances and mortality. If significant associations were to be found, then there will be a need to determine why outpatient appointments are not attended. The day of the week or time of day of scheduled appointments could be factors for missed appointments. Ellis and Jenkins (2012) in Scotland found DNA highest on Mondays and lowest on Fridays, particularly for younger age groups (297). Qualitative methods would also be useful in finding out why appointments are missed.

7.5 Conclusion.

This study has shown that analysis of routine datasets provides empirical evidence for the need of extra support for individuals diagnosed with an LTC during the transitional care period to prevent negative long-term health outcomes. It suggests that current mental health services provisions may not be adequately addressed, particularly for those diagnosed during the transitional care period. Older age groups in the transitional care period also need greater attention. Previous research into the transitional care period tends to focus on ages under 25 years. This study shows that individuals over this age should not be overlooked. Socio-demographic factors should also be considered for targeted interventions.

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Appendix A: International classification of childhood and young adult cancer.

A.1 Classification scheme for cancers in children (22).

Group 1 - Leukaemias, myeloproliferative diseases, and myelodysplastic diseases

1.1. Lymphoid leukaemias

1.2. Acute myeloid leukaemias

1.3. Chronic myeloproliferative diseases

1.4. Myelodysplastic syndrome and other myeloproliferative diseases

1.5. Unspecified and other specified leukaemias

Group 2 - Lymphomas and reticuloendothelial neoplasms

2.1. Hodgkin lymphomas

2.2. Non-Hodgkin lymphomas (except Burkitt lymphoma)

2.3. Burkitt lymphoma

2.4. Miscellaneous lymphoreticular neoplasms e. Unspecified lymphomas

Group 3 - CNS and miscellaneous intracranial and intraspinal neoplasms

1.1. Ependymomas and choroid plexus tumour

1.2. Astrocytomas

3.3. Intracranial and intraspinal embryonal tumours

3.4. Other gliomas

3.5. Other specified intracranial and intraspinal neoplasms

3.6. Unspecified intracranial and intraspinal neoplasms

Group 4 - Neuroblastoma and other peripheral nervous cell tumours

4.1. Neuroblastoma and ganglioneuroblastoma

4.2. Other peripheral nervous cell tumours

Group 5 – Retinoblastoma

Group 6 - Renal tumours

6.1. Nephroblastoma and other nonepithelial renal tumours

6.2. Renal carcinomas

6.3. Unspecified malignant renal tumours

Group 7 - Hepatic tumours

7.1. Hepatoblastoma

7.2. Hepatic carcinomas

7.3. Unspecified malignant hepatic tumours

Group 8 - Malignant bone tumours

8.1. Osteosarcomas

8.2. Chondrosarcomas

8.3. Ewing tumour and related sarcomas of bone

8.4. Other specified malignant bone tumours

8.5. Unspecified malignant bone tumours

Group 9 - Soft tissue and other extraosseous sarcomas

9.1. Rhabdomyosarcomas

9.2. Fibrosarcomas, peripheral nerve sheath tumours, and other fibrous neoplasms

9.3. Kaposi sarcoma

9.4. Other specified soft tissue sarcomas

9.5. Unspecified soft tissue sarcomas

Group 10 - Germ cell tumours, trophoblastic tumours, and neoplasms of gonads

10.1. Intracranial and intraspinal germ cell tumours

10.2. Malignant extracranial and extragonadal germ cell tumours

10.3. Malignant gonadal germ cell tumours

10.4. Gonadal carcinomas

10.5. Other and unspecified malignant gonadal tumours

Group 11 - Other malignant epithelial neoplasms and malignant melanomas

11.1. Adrenocortical carcinomas

11.2. Thyroid carcinomas

11.3. Nasopharyngeal carcinomas

11.4. Malignant melanomas

11.5. Skin carcinomas

11.6. Other and unspecified carcinomas

Group 12 - Other and unspecified malignant neoplasms

12.1. Other specified malignant tumours

12.2. Other unspecified malignant tumours

A.2 Classification scheme for cancers in adolescents and young adults (23).

Group 1 – Leukaemias

1.1. Acute lymphoid leukaemia (ALL)

1.2. Acute myeloid leukaemia (AML)

1.3. Chronic myeloid leukaemia (CML)

1.4. Other and unspecified leukaemia (Other Leuk)

1.4.1. Other and unspecified lymphoid leukaemias

1.4.2. Other and unspecified myeloid leukaemias

1.4.3. Other specified leukaemias, NEC

1.4.4. Unspecified leukaemia

Group 2 – Lymphomas

2.1. Non-Hodgkin's lymphoma (NHL)

2.1.1. Non-Hodgkin's lymphoma, specified subtype

2.1.2. Non-Hodgkin's lymphoma, subtype not specified

2.2. Hodgkin's disease (HD)

2.2.1. Hodgkin's disease, specified subtype

2.2.2. Hodgkin's disease, subtype not specified

Group 3 – Central nervous system and other intracranial and intraspinal neoplasms (CNS tumours)

3.1. Astrocytoma

3.1.1. Specified low grade astrocytoma

3.1.2. Glioblastoma and anaplastic astrocytoma

3.1.3. Astrocytoma not otherwise specified

3.2. Other gliomas

3.3. Ependymoma

3.4. Medulloblastoma and other primitive neuroectodermal tumours (Medulloblastoma)

3.5. Other and unspecified malignant intracranial and intraspinal neoplasms (Other CNS)

3.5.1. Other specified malignant intracranial and intraspinal neoplasms

3.5.2. Unspecified malignant intracranial and intraspinal neoplasms

3.6. Non-malignant intracranial and intraspinal neoplasms

3.6.1. Specified non-malignant intracranial or intraspinal neoplasms

3.6.2. Unspecified intracranial or intraspinal neoplasms

Group 4 – Osseous and chondromatous neoplasms, Ewings tumour and other neoplasms of bone (bone tumours)

4.1. Osteosarcoma

4.2. Chondrosarcoma

4.3. Ewing's tumour

4.4. Other specified and unspecified bone tumours (Other bone tumours)

4.4.1. Other specified bone tumours

4.4.2. Unspecified bone tumours

Group 5 – Soft tissue sarcomas (STS)

5.1. Fibromatous neoplasms (Fibrosarcoma)

5.2. Rhabdomyosarcoma

5.3. Other soft tissue sarcomas

5.3.1. Other specified soft tissue sarcomas

5.3.2. Unspecified soft tissue sarcomas

Group 6 – Germ cell and trophoblastic neoplasms (germ cell tumours)

6.1. Gonadal germ cell and trophoblastic neoplasms

6.2. Germ cell and trophoblastic neoplasms of non-gonadal sites

6.2.1. Intracranial germ cell and trophoblastic tumours

6.2.2. Other non-gonadal germ cell and trophoblastic tumours

Group 7 – Melanoma and skin carcinoma

7.1. Melanoma

7.2. Skin carcinoma

Group 8 – Carcinomas (except of skin)

8.1. Carcinoma of thyroid

8.2. Other carcinoma of head and neck

8.2.1. Nasopharyngeal carcinoma

8.2.2. Carcinoma of other sites in lip oral cavity and pharynx

8.2.3. Carcinoma of nasal cavity, middle ear, sinuses, larynx and other ill-defined sites in head and neck

8.3. Carcinoma of trachea, bronchus, lung and pleura

8.4. Carcinoma of breast

8.5. Carcinoma of genito-urinary (GU) tract

8.5.1. Carcinoma of kidney

8.5.2. Carcinoma of bladder

8.5.3. Carcinoma of ovary and testis

8.5.4. Carcinoma of cervix and uterus

8.5.5. Carcinoma of other and ill-defined sites in GU

8.6. Carcinoma of gastro-intestinal (GI) tract

8.6.1. Carcinoma of colon and rectum

8.6.2. Carcinoma of stomach

8.6.3. Carcinoma of liver and ill-defined sites in GI tract

8.7. Carcinomas of other and ill-defined sites not elsewhere classified (NEC)

8.7.1. Adrenocortical carcinoma

8.7.2. Other carcinomas NEC

Group 9 – Miscellaneous specified neoplasms NEC

9.1. Embryonal tumours NEC

9.1.1. Wilms tumour

9.1.2. Neuroblastoma

9.1.3. Other embryonal tumours NEC

9.2. Other rare miscellaneous specified neoplasms

9.2.1. Paraganglioma and glomus tumours

9.2.2. Other specified gonadal tumours NEC

9.2.3. Myeloma, mast cell tumours and miscellaneous reticuloendothelial neoplasms NEC

9.2.4 Other specified neoplasms NEC

Group 10 – Unspecified malignant neoplasms NEC

Appendix B: Literature search strategies.

Table B.1: Search strategy for the topic of 'transition'.

Stage	Search term	Results – EMBASE	Results – Medline
1	transition to adult care/	1,420	1,028
2	limit 1 to human	1,411	1,026
3	limit 2 to English language	1,321	951
4	limit 3 to full text	344	177
5	limit 4 to article	148	152
	Manual selection	105	

Exclusions during manual selection included:

- adolescent health with no mention of transition
- transitioning between departments, not specifically between paediatric to adult services
- pilot studies and protocols
- editorials
- case studies

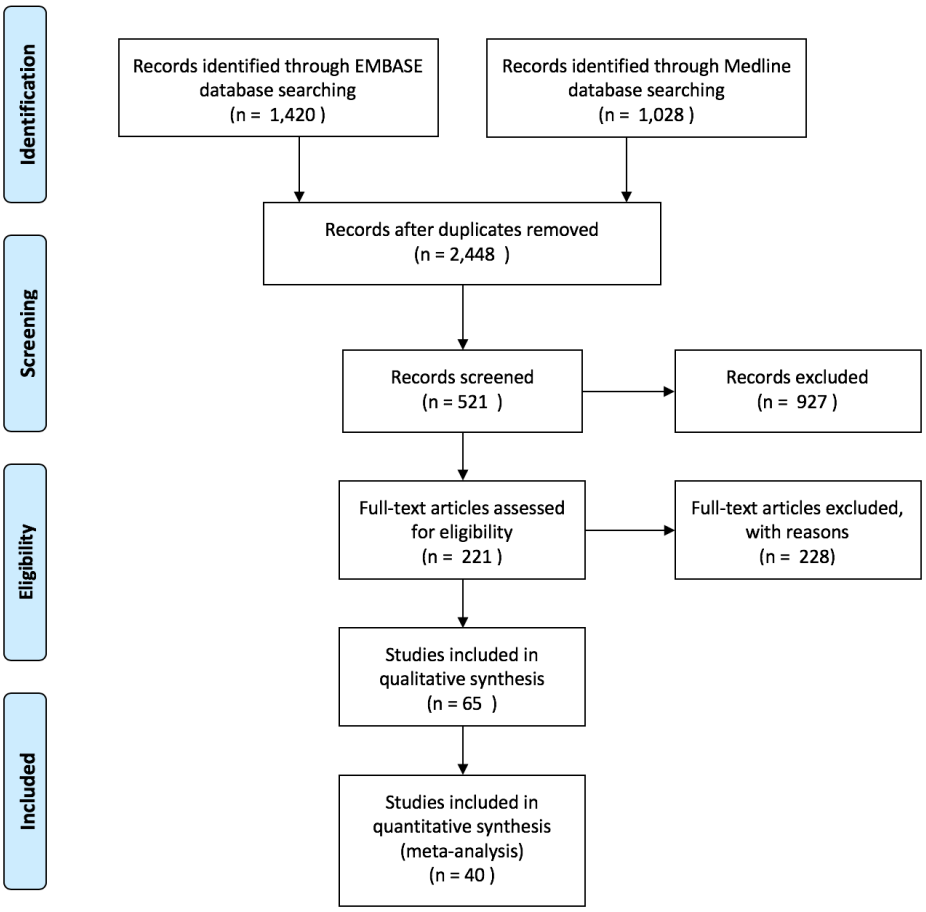


Figure B.1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for literature search on transition.

Table B.2: Search strategy for the topic of 'T1D outcomes'.

Stage	Search term – EMBASE	Results - EMBASE	Search term – Medline	Results - Medline
1	insulin dependent diabetes mellitus/	69833	Diabetes Mellitus, Type 1/	41993
2	diabetic angiopathy/ or diabetic cardiomyopathy/ or diabetic coma/ or diabetic foot/ or diabetic hypertension/ or diabetic ketoacidosis/ or diabetic macular edema/ or diabetic nephropathy/ or diabetic neuropathy/ or diabetic	99272	Diabetes Complications/	21506

	obesity/ or diabetic retinopathy/ or diabetic stomach paresis/ or nonketotic diabetic coma/ or pregnancy diabetes mellitus/			
3	1 and 2	13459	1 and 2	1133
4	limit 3 to human	12485	limit 3 to human	1100
5	limit 4 to English language	11014	limit 4 to English language	899
6	limit 5 to full text	3684	limit 5 to full text	307
7	limit 6 to article	2033	limit 6 to article	277
8	limit 7 to last 5 years	579	limit 7 to last 5 years	99
	Manual selection		70	

Exclusions during manual selection included:

- case reports
- treatment trials
- screening research
- no separation from type 2 diabetes
- where T1D is a supplementary disease
- comorbidity with other diseases

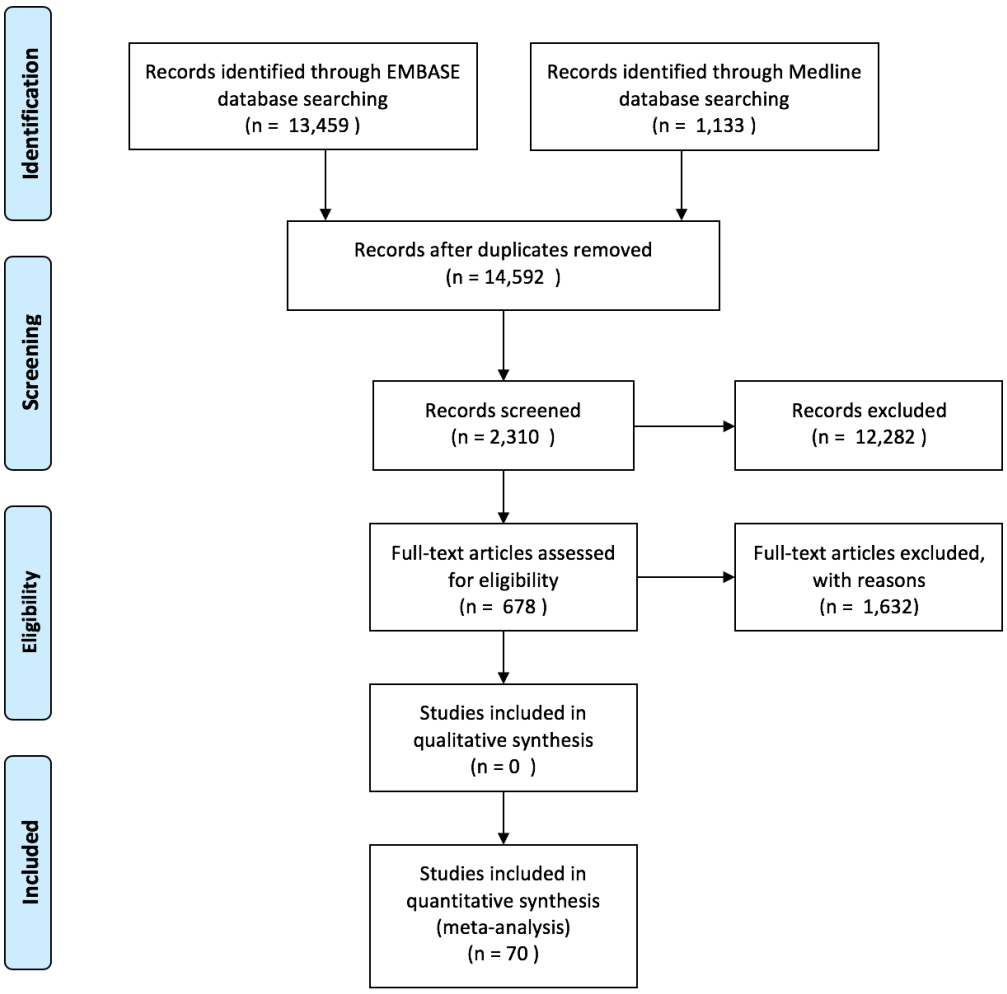


Figure B.2: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for literature search on type 1 diabetes (T1D).

Table B.3: Search strategy for the topic of 'childhood cancer outcomes'.

Stage	Search term – EMBASE	Results - EMBASE	Search term – Medline	Results - Medline
1	childhood cancer/	22951	Neoplasms/	186425
2	late effect*.mp.	6264	Child/ or Infant/	922800
3	early effect*.mp.	2906	1 and 2	12341
4	outcome*.mp.	2158957	late effect*.mp.	3423
5	complication*.mp.	993203	early effect*.mp.	1932
6	follow?up.mp.	28455	outcome*.mp.	1490835
7	long?term.mp.	14702	complication*.mp.	652315
8	surviv*.mp.	1183991	follow?up.mp.	12660
9	2 or 3 or 4 or 5 or 6 or 7 or 8	3615707	long?term.mp.	2949
10	1 and 9	11911	surviv*.mp.	799888
11	limit 10 to human	10814	3 or 4 or 5 or 6 or 7 or 8 or 9 or 10	2437305
12	limit 11 to English language	10225	3 and 11	4823
13	limit 12 to full text	2869	limit 12 to human	4823
14	limit 13 to article	1530	limit 13 to English language	4418
15	limit 14 to last 5 years	454	limit 14 to full text	1323
16			limit 15 to article	1265
17			limit 16 to last 5 years	344
	Manual selection		48	

Exclusions during manual selection included:

- case reports
- treatment trials
- research on screening

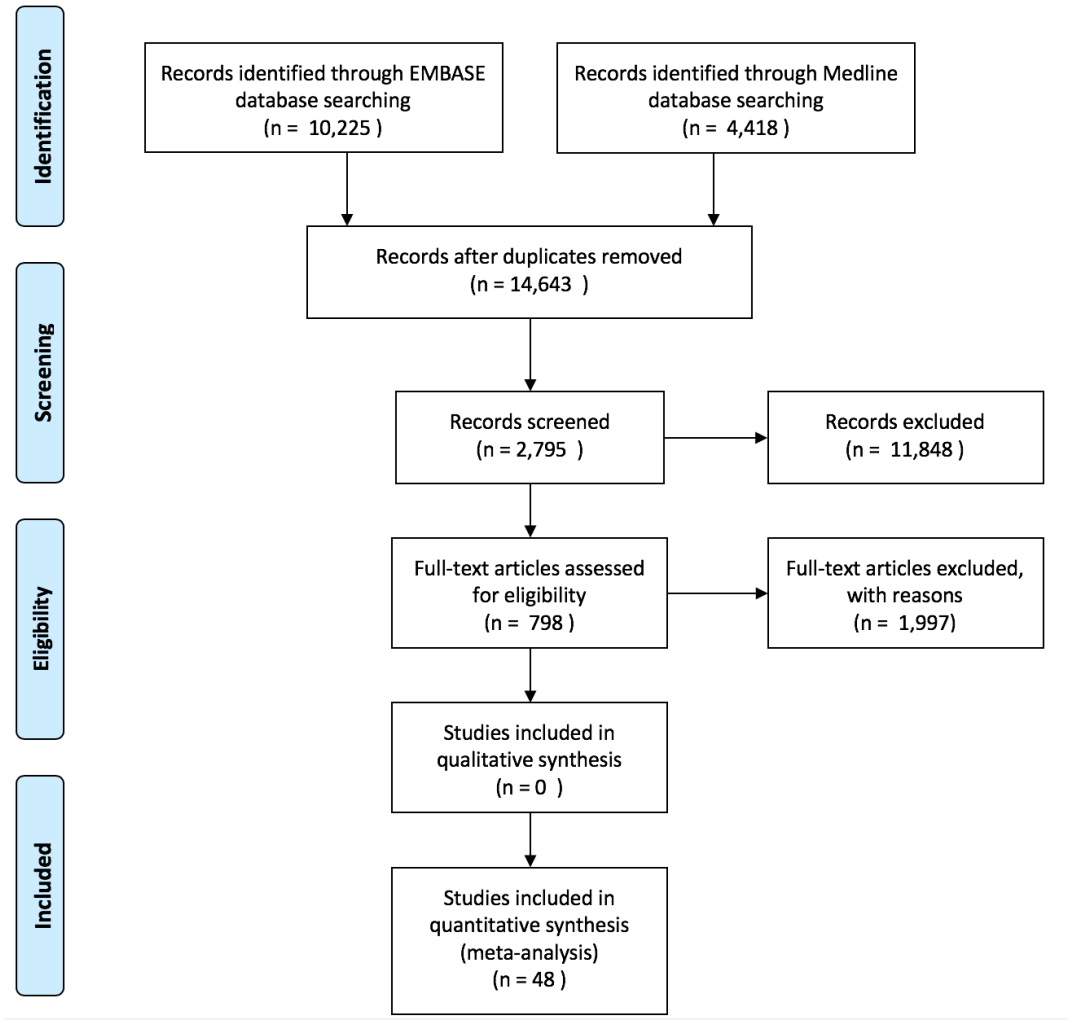


Figure B.3: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart for literature search on cancer.

Appendix C: Model fit comparisons for multi-level models using data from the Leeds Children and Young People's Diabetes Service (LCYPDS) cohort.

Both the Akaike's Information Criterion and Bayesian Information Criterion were lower for the random intercept model, indicating that this was a better fitting model compared with the random slope mode (Table C.1).

Table C.1: Akaike's Information Criterion and Bayesian Information Criterion for random intercept and random slope models comparing individuals who continued within individuals who discontinued continuous subcutaneous insulin infusion (CSII) therapy.

Multi-level model	Akaike's Information Criterion	Bayesian Information Criterion
Random intercept model	6476.524	6516.391
Random slope model	6476.854	6522.416

Appendix D: International classification of Diseases (ICD).

Table D.1: International Statistical Classification of Diseases and Related Health Problems 10th Revision.

Chapter	Blocks	Title
I	A00-B99	Certain infectious and parasitic diseases
II	C00-D48	Neoplasms
III	D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
IV	E00-E90	Endocrine, nutritional and metabolic diseases
V	F00-F99	Mental and behavioural disorders
VI	G00-G99	Diseases of the nervous system
VII	H00-H59	Diseases of the eye and adnexa
VIII	H60-H95	Diseases of the ear and mastoid process
IX	I00-I99	Diseases of the circulatory system
X	J00-J99	Diseases of the respiratory system
XI	K00-K93	Diseases of the digestive system
XII	L00-L99	Diseases of the skin and subcutaneous tissue
XIII	M00-M99	Diseases of the musculoskeletal system and connective tissue
XIV	N00-N99	Diseases of the genitourinary system
XV	O00-O99	Pregnancy, childbirth and the puerperium
XVI	P00-P96	Certain conditions originating in the perinatal period
XVII	Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities
XVIII	R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
XIX	S00-T98	Injury, poisoning and certain other consequences of external causes
XX	V01-Y98	External causes of morbidity and mortality
XXI	Z00-Z99	Factors influencing health status and contact with health services
XXII	U00-U99	Codes for special purposes

Appendix E: Treatment specialty groupings in Hospital Episode Statistics (HES)

Table E.1: Treatment specialty groupings.

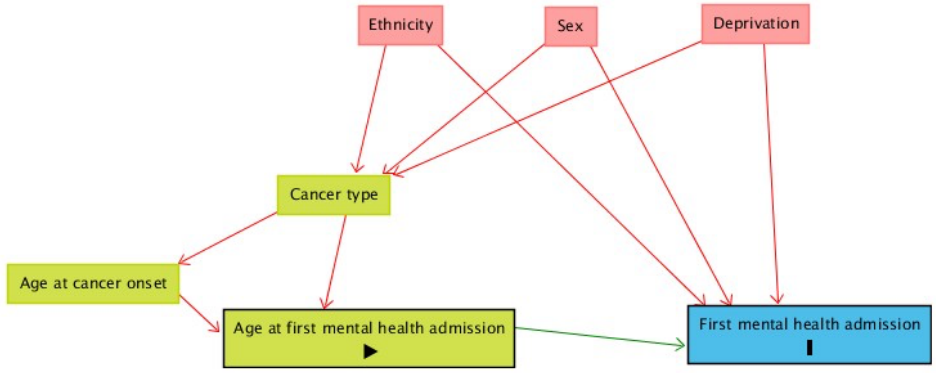
HES code	HES category	New category
324	Anticoagulant Service	circulatory
320	Cardiology	circulatory
321	Paediatric Cardiology	circulatory
107	Vascular Surgery	circulatory
170	Cardiothoracic Surgery (Where There Are No Separate Services For Cardiac And Thoracic Surgery)	circulatory
221	Paediatric Cardiac Surgery (From 2006-07)	circulatory
331	Congenital Heart Disease Service (From April 2013)	circulatory
174	Cardiothoracic Transplantation (Recognised Specialist Services Only - Includes 'Outreach' Facilities)	circulatory
654	Dietetics (From 2006-07)	digestion
301	Gastroenterology	digestion
251	Paediatric Gastroenterology (From 2006-07)	digestion
306	Hepatology	digestion
104	Colorectal Surgery (Surgical Treatment Of Disorders Of The Lower Intestine - Colon, Anus And Rectum)	digestion
106	Upper Gastrointestinal Surgery	digestion
105	Hepatobiliary & Pancreatic Surgery (Includes Liver Surgery But Excludes Liver Transplantation See Transplantation Surgery)	digestion
840	Audiology (From 2008-09)	ears, nose, throat
310	Audiological Medicine	ears, nose, throat
254	Paediatric Audiological Medicine (From 2006-07)	ears, nose, throat
120	Ear, Nose And Throat (Ent)	ears, nose, throat
215	Paediatric Ear Nose And Throat (From 2006-07)	ears, nose, throat
302	Endocrinology	endocrinology
252	Paediatric Endocrinology (From 2006-07)	endocrinology
307	Diabetic Medicine	endocrinology
263	Paediatric Diabetic Medicine	endocrinology
261	Paediatric Metabolic Disease (From 2006-07)	endocrinology
130	Ophthalmology	eyes
216	Paediatric Ophthalmology (From 2006-07)	eyes
460	Medical Ophthalmology (From 1993-94)	eyes
662	Optometry	eyes
255	Paediatric Clinical Immunology And Allergy (From 2006-07)	immunology/allergy
313	Clinical Immunology And Allergy (Where There Are No Separate Services For Clinical Immunology And Allergy)	immunology/allergy

316	Clinical Immunology	immunology/allergy
317	Allergy Service	immunology/allergy
830	Immunopathology	immunology/allergy
110	Trauma And Orthopaedics	joints/muscles/skin
330	Dermatology	joints/muscles/skin
650	Physiotherapy (From 2006-07)	joints/muscles/skin
410	Rheumatology	joints/muscles/skin
214	Paediatric Trauma And Orthopaedics (From 2006-07)	joints/muscles/skin
257	Paediatric Dermatology (From 2006-07)	joints/muscles/skin
323	Spinal Injuries (From 2006-07)	joints/muscles/skin
262	Paediatric Rheumatology (From 2006-07)	joints/muscles/skin
161	Burns Care (Recognised Specialist Services Only - Includes 'Outreach' Facilities)	joints/muscles/skin
657	Prosthetics	joints/muscles/skin
325	Sport And Exercise Medicine	joints/muscles/skin
655	Orthoptics (From 2006-07)	joints/muscles/skin
658	Orthotics	joints/muscles/skin
108	Spinal Surgery Service (From April 2013)	joints/muscles/skin
501	Obstetrics For Patients Using A Hospital Bed Or Delivery Facilities	maternity/obstetrics/gynaecology
502	Gynaecology	maternity/obstetrics/gynaecology
560	Midwifery Service	maternity/obstetrics/gynaecology
560	Midwifery (From October 1995)	maternity/obstetrics/gynaecology
503	Gynaecological Oncology	maternity/obstetrics/gynaecology
422	Neonatology	maternity/obstetrics/gynaecology
424	Well Babies (Care Given By The Mother/Substitute, With Nursing Advice If Needed)	maternity/obstetrics/gynaecology
710	Adult Mental Illness	mental health
656	Clinical Psychology (From 2006-07)	mental health
711	Child And Adolescent Psychiatry	mental health
713	Psychotherapy	mental health
720	Eating Disorders (From 2006-07)	mental health
101	Urology	nephrology
361	Nephrology	nephrology
259	Paediatric Nephrology (From 2006-07)	nephrology
360	Genitourinary Medicine	nephrology
360	Genito-Urinary Medicine	nephrology
211	Paediatric Urology (From 2006-07)	nephrology
328	Stroke Medicine	neurology
329	Transient Ischaemic Attack	neurology
400	Neurology	neurology
150	Neurosurgery	neurology
421	Paediatric Neurology	neurology
218	Paediatric Neurosurgery (From 2006-07)	neurology
291	Paediatric Neuro-Disability (From 2006-07)	neurology
652	Speech And Language Therapy (From 2006-07)	neurology
700	Learning Disability (Previously Known As Mental Handicap)	neurology
223	Paediatric Epilepsy (From April 2013)	neurology
401	Clinical Neurophysiology (From 2008-09)	neurology
401	Clinical Neuro-Physiology	neurology
309	Haemophilia (Previously Part Of Clinical	oncology

	Haematology)	
260	Paediatric Medical Oncology (From 2006-07)	oncology
303	Clinical Haematology	oncology
303	Haematology (Clinical)	oncology
370	Medical Oncology	oncology
800	Clinical Oncology (Previously Known As Radiotherapy)	oncology
823	Haematology	oncology
253	Paediatric Clinical Haematology (From 2006-07)	oncology
308	Bone And Marrow Transplantation (Previously Part Of Clinical Haematology)	oncology
140	Oral Surgery	oral health
143	Orthodontics	oral health
142	Paediatric Dentistry (From 1999-2000)	oral health
141	Restorative Dentistry (Endodontics, Periodontics And Prosthodontics)	oral health
144	Maxillo-Facial Surgery	oral health
450	Dental Medicine (From 1990-91)	oral health
217	Paediatric Maxillo-Facial Surgery (From 2006-07)	oral health
191	Pain Management (Complex Pain Disorders Requiring Diagnosis And Treatment By A Specialist Multi-Professional Team)	other
241	Paediatric Pain Management (From 2006-07)	other
653	Podiatry (From 2006-07)	other
314	Rehabilitation Service	other
344	Complex Specialised Rehabilitation Service (From April 2013)	other
345	Specialist Rehabilitation Service (From April 2013)	other
180	Accident & Emergency (A&E)	other
430	Geriatric Medicine	other
822	Chemical Pathology	other
304	Clinical Physiology (From 2008-09)	other
420	Paediatrics	other
300	General Medicine	other
950	Nursing Episode (From 2002-03)	other
290	Community Paediatrics (From 2006-07)	other
820	General Pathology	other
900	Community Medicine	other
305	Clinical Pharmacology	other
311	Clinical Genetics	other
812	Diagnostic Imaging (From 2008-09)	other
811	Interventional Radiology	other
371	Nuclear Medicine (From 2008-09)	other
810	Radiology	other
350	Infectious Diseases	other
192	Critical Care Medicine (Also Known As Intensive Care Medicine)	other
651	Occupational Therapy (From 2006-07)	other
315	Palliative Medicine	other
264	Paediatric Cystic Fibrosis	respiratory
343	Adult Cystic Fibrosis Service	respiratory

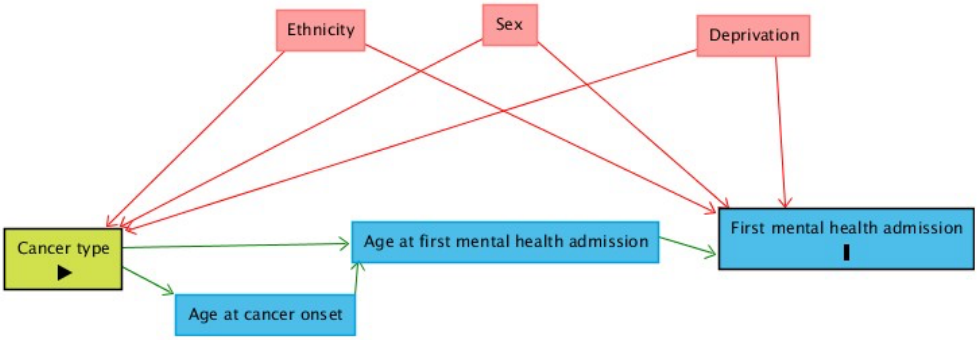
340	Respiratory Medicine (Previously Known As Thoracic Medicine)	respiratory
340	Thoracic Medicine	respiratory
258	Paediatric Respiratory Medicine (From 2006-07)	respiratory
341	Respiratory Physiology (Previously Known As Sleep Studies)	respiratory
173	Thoracic Surgery	respiratory
190	Anaesthetics	surgery
100	General Surgery	surgery
160	Plastic Surgery	surgery
103	Breast Surgery (Includes Suspected Neoplasms, Cysts Etc, Does Not Include Cosmetic Surgery)	surgery
171	Paediatric Surgery	surgery
102	Transplantation Surgery (Includes Renal And Liver Transplants, Excludes Cardiothoracic Transplantation)	surgery
212	Paediatric Transplantation Surgery (From 2006-07)	surgery
219	Paediatric Plastic Surgery (From 2006-07)	surgery

Appendix F: Directed acyclic graphs (DAGs) for statistical models used in analysis of the Yorkshire Specialist Register of Cancer in Children and Young People



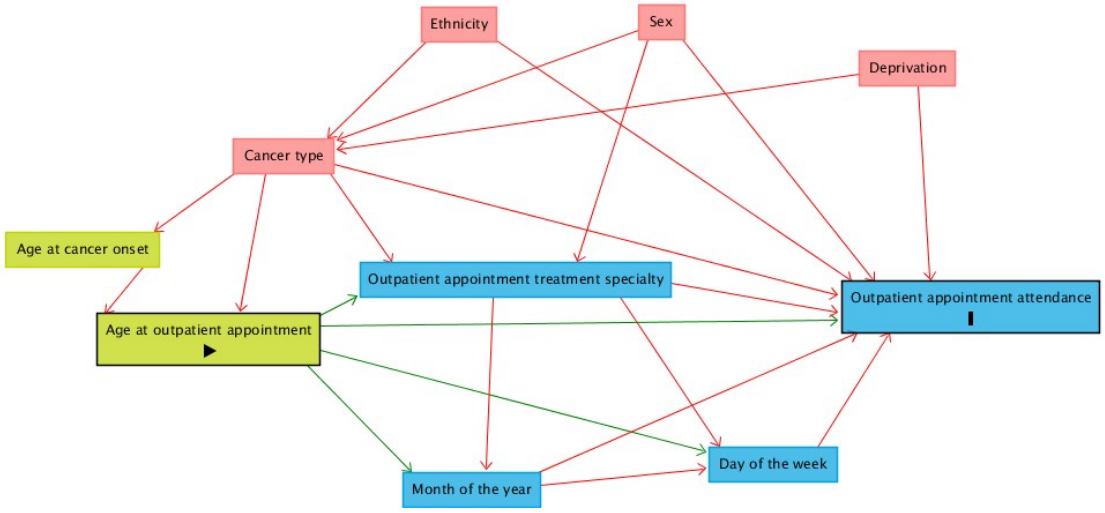
Confounders: ethnicity, sex, deprivation.
Proxy confounders: Age at cancer onset, cancer type.

Figure F.1: Mental health admission - age at first mental health admission.



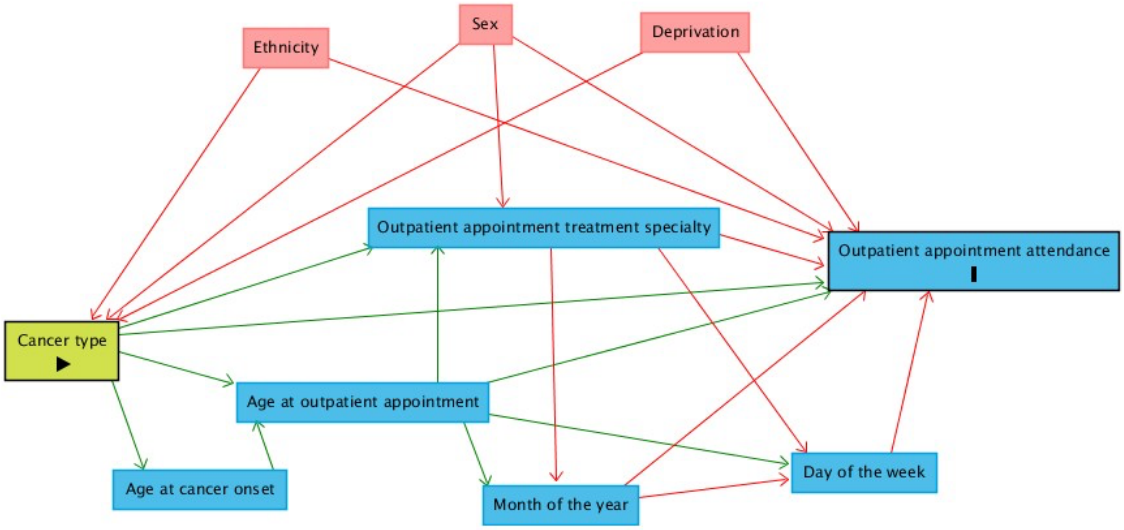
Confounders: ethnicity, sex, deprivation.
Mediators: Age at cancer onset, age at first mental health admission.

Figure F.2: Mental health admission - cancer type.



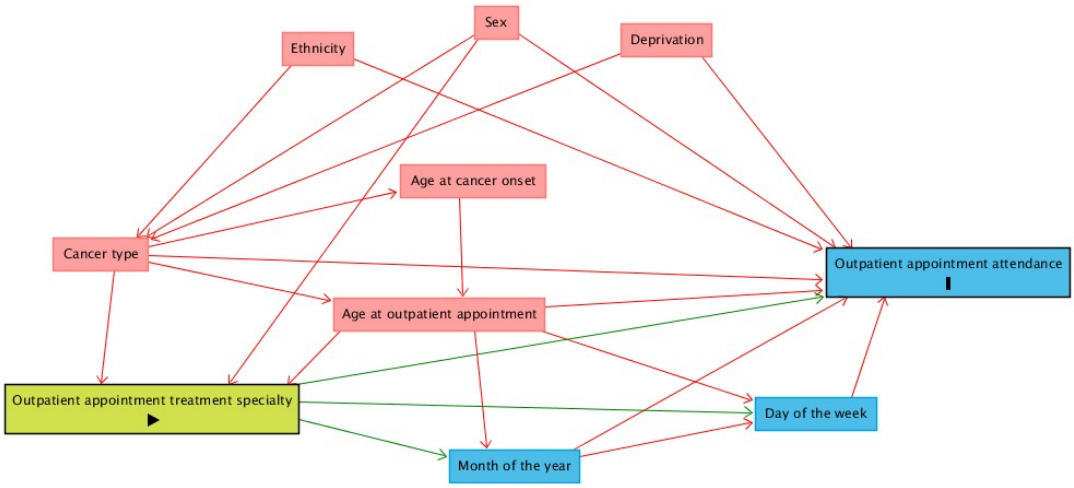
Confounders: ethnicity, sex, deprivation.
Proxy confounders: Age at cancer onset, cancer type.
Mediators: Outpatient appointment treatment specialty, month of the year, day of the week.

Figure F.3: Outpatient attendance - age at outpatient appointment.



Confounders: ethnicity, sex, deprivation.
Mediators: Outpatient appointment treatment specialty, age at outpatient appointment, age at cancer onset, month of the year, day of the week.

Figure F.4: Outpatient appointment attendance - cancer type.

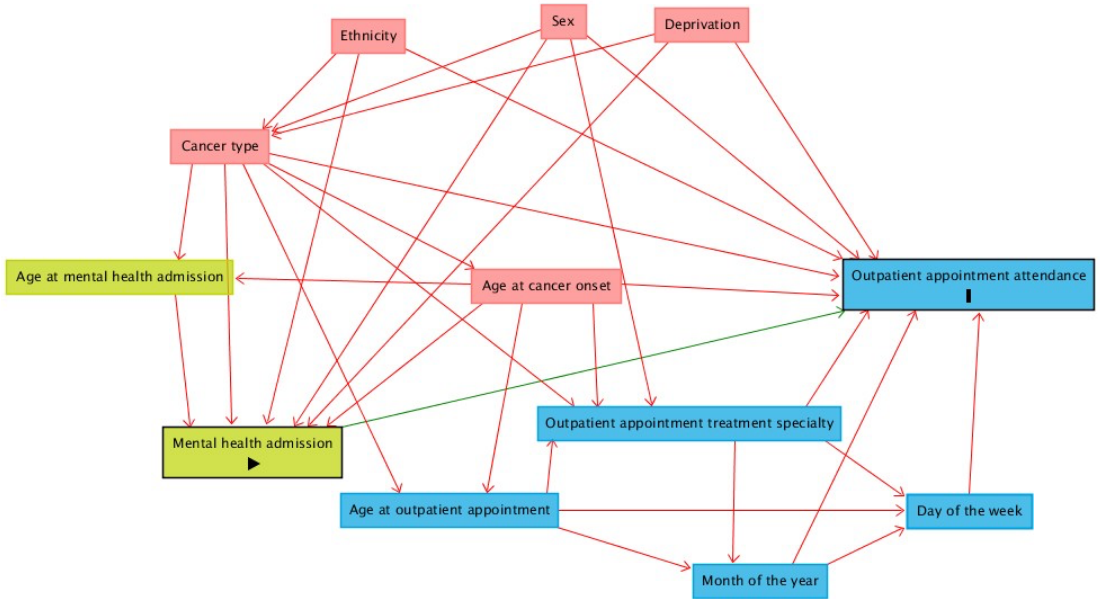


Confounders: ethnicity, sex, deprivation.

Proxy confounders: Age at cancer onset, cancer type, age at outpatient appointment.

Mediators: month of the year, day of the week.

Figure F.5: Outpatient appointment attendance - treatment specialty.

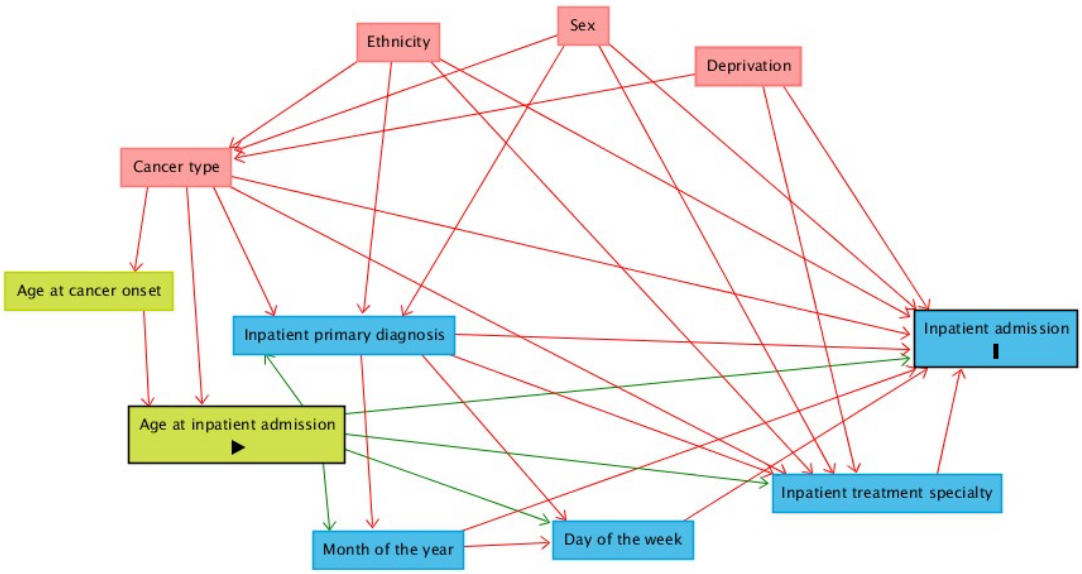


Confounders: ethnicity, sex, deprivation.

Proxy confounders: Age at cancer onset, cancer type age at mental health admission.

Competing exposures: Outpatient appointment treatment specialty, age at outpatient appointment, month of the year, day of the week.

Figure F.6: Outpatient appointment attendance - mental health admission.

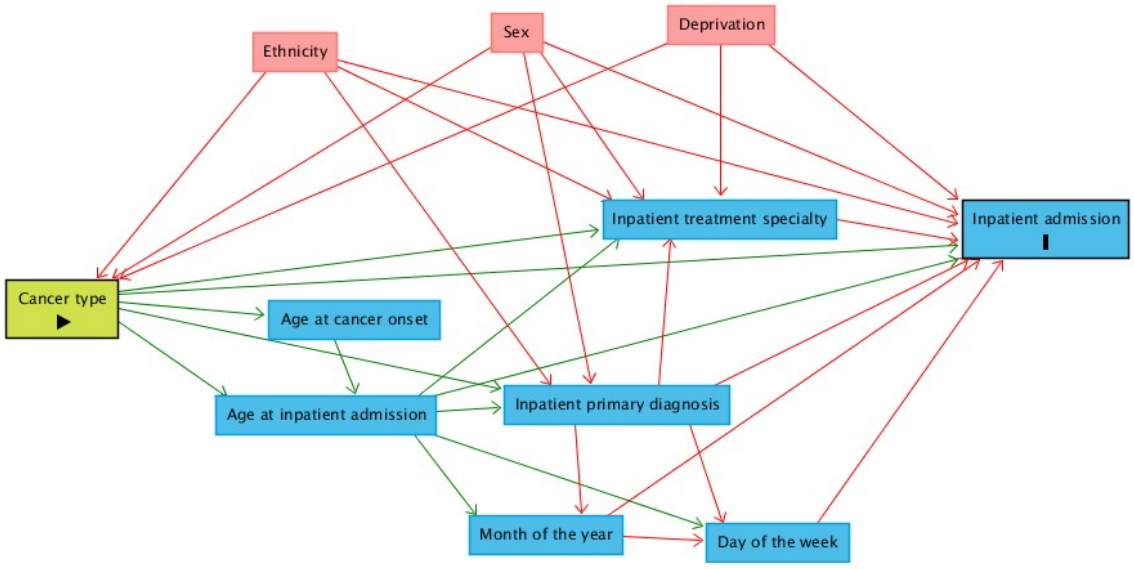


Confounders: ethnicity, sex, deprivation.

Proxy confounders: Age at cancer onset, cancer type age at mental health admission.

Mediators: Inpatient primary diagnosis, inpatient treatment specialty, month of the year, day of the week.

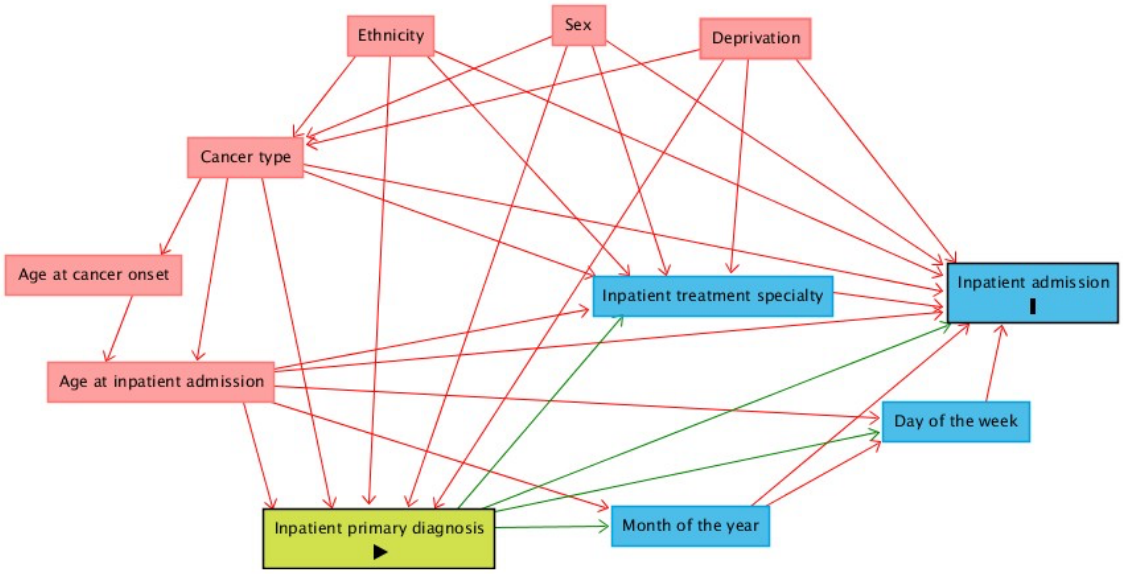
Figure F.7: Inpatient admission - age at inpatient attendance.



Confounders: ethnicity, sex, deprivation.

Mediators: Age at cancer onset, age at inpatient admission, inpatient primary diagnosis, inpatient treatment specialty, month of the year, day of the week.

Figure F.8: Inpatient admission - cancer type.

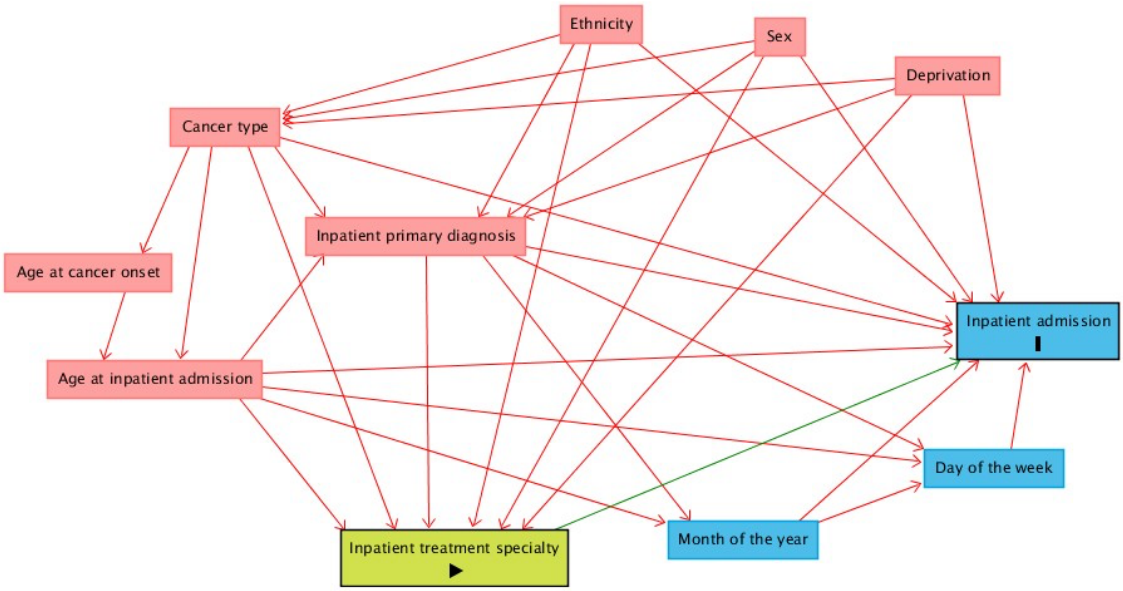


Confounders: ethnicity, sex, deprivation.

Proxy confounders: cancer type, age at cancer onset, age at inpatient admission.

Mediators: inpatient treatment specialty, month of the year, day of the week.

Figure F.9: Inpatient admission - inpatient primary diagnosis.

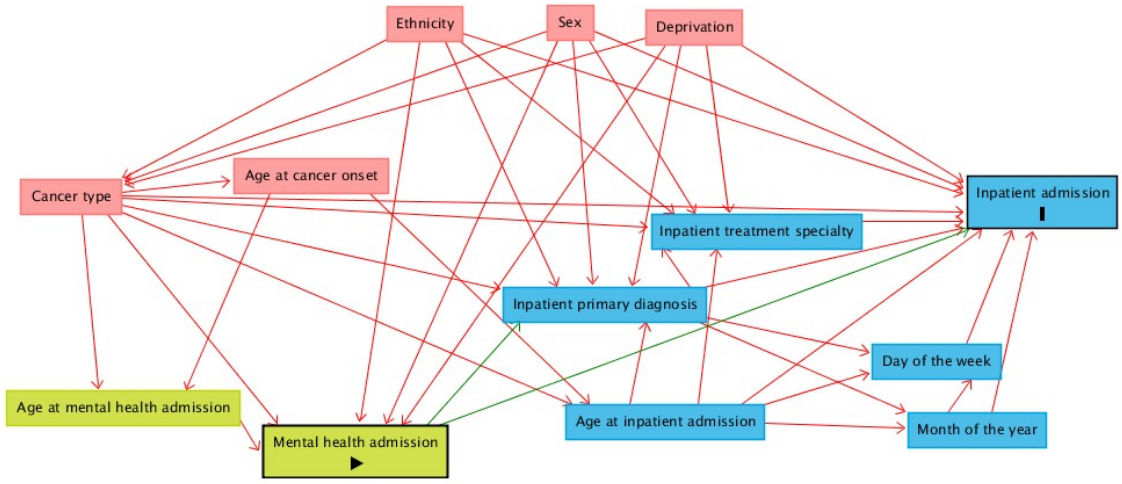


Confounders: ethnicity, sex, deprivation.

Proxy confounders: cancer type, age at cancer onset, age at inpatient admission, inpatient primary diagnosis.

Competing exposures: month of the year, day of the week.

Figure F.10: Inpatient admission - inpatient treatment specialty.



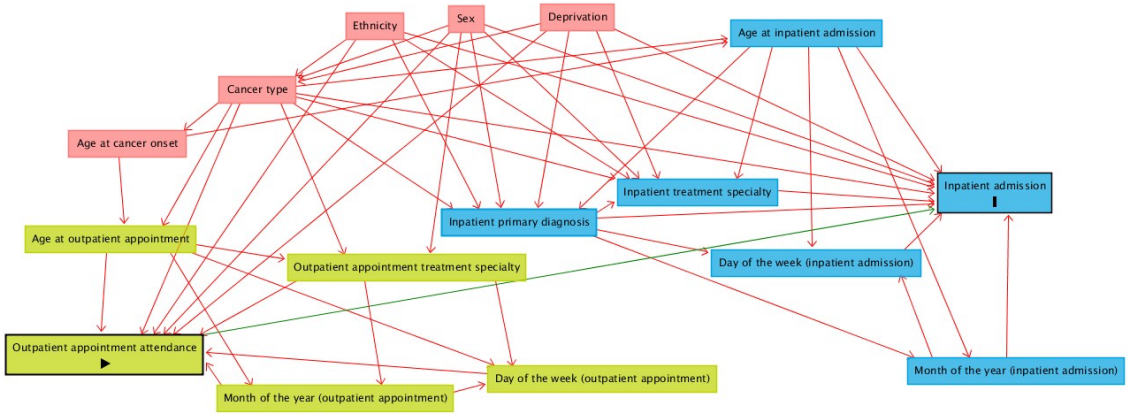
Confounders: ethnicity, sex, deprivation.

Proxy confounders: cancer type, age at cancer onset, age at mental health admission.

Mediators: inpatient primary diagnosis, inpatient treatment specialty, month of the year, day of the week.

Competing exposure: age at inpatient admission.

Figure F.11: Inpatient admission - mental health admission.

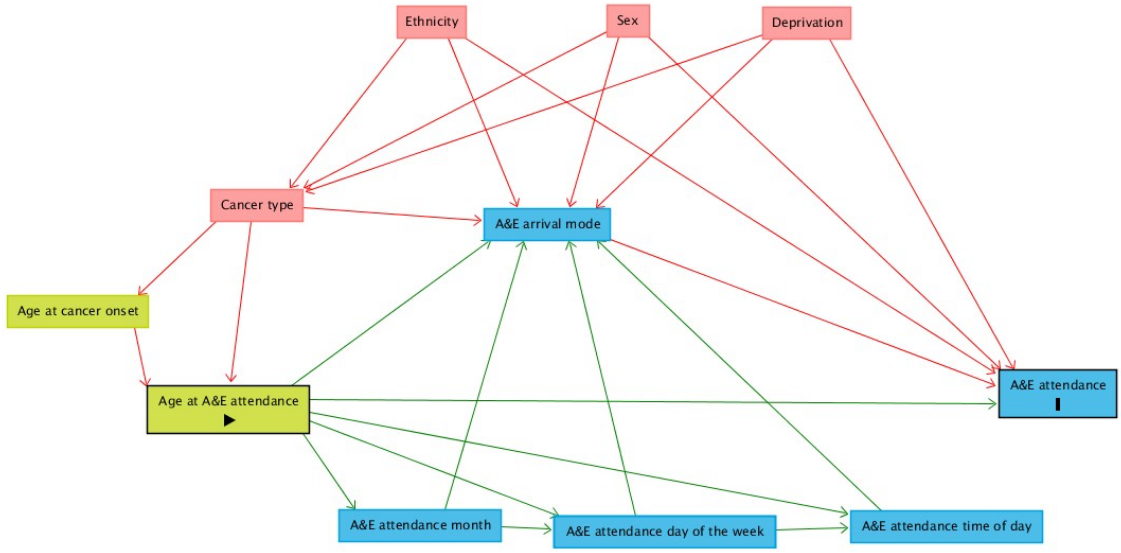


Confounders: ethnicity, sex, deprivation.

Proxy confounders: cancer type, age at cancer onset, age at outpatient appointment, outpatient appointment treatment specialty, month of the year (outpatient appointment), day of the week (outpatient appointment).

Competing exposures: inpatient primary diagnosis, age at inpatient admission, inpatient treatment specialty, month of the year (inpatient admission), day of the week (inpatient admission).

Figure F.12: Inpatient admission - outpatient appointment attendance.

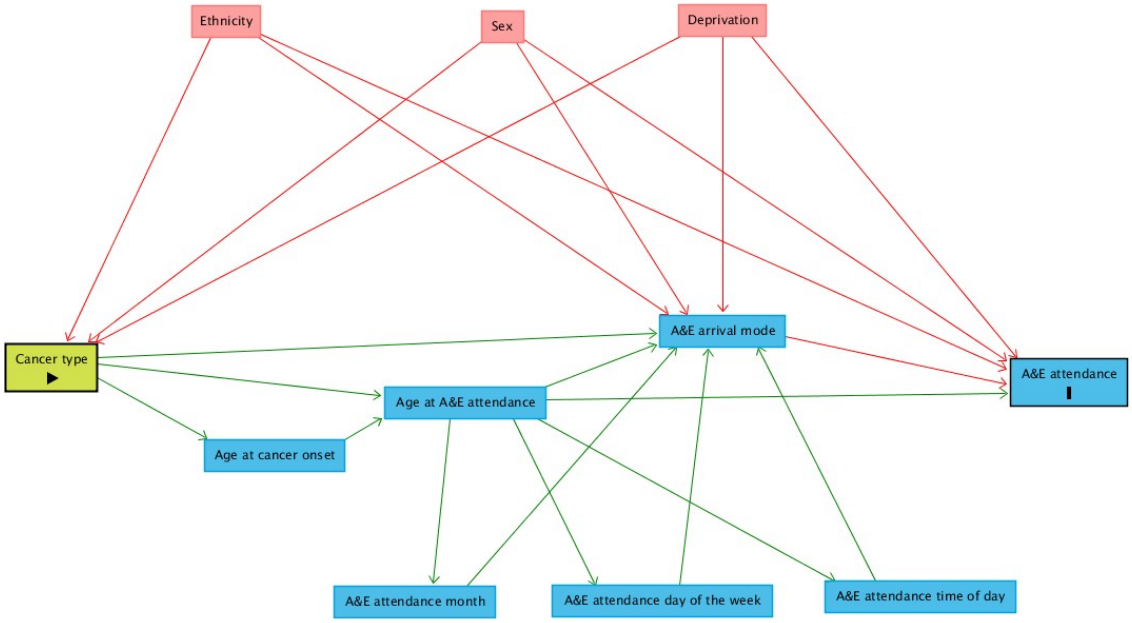


Confounders: ethnicity, sex, deprivation.

Proxy confounders: cancer type, age at cancer onset.

Mediators: A&E arrival mode, A&E attendance month, A&E attendance day of the week, A&E attendance time of day.

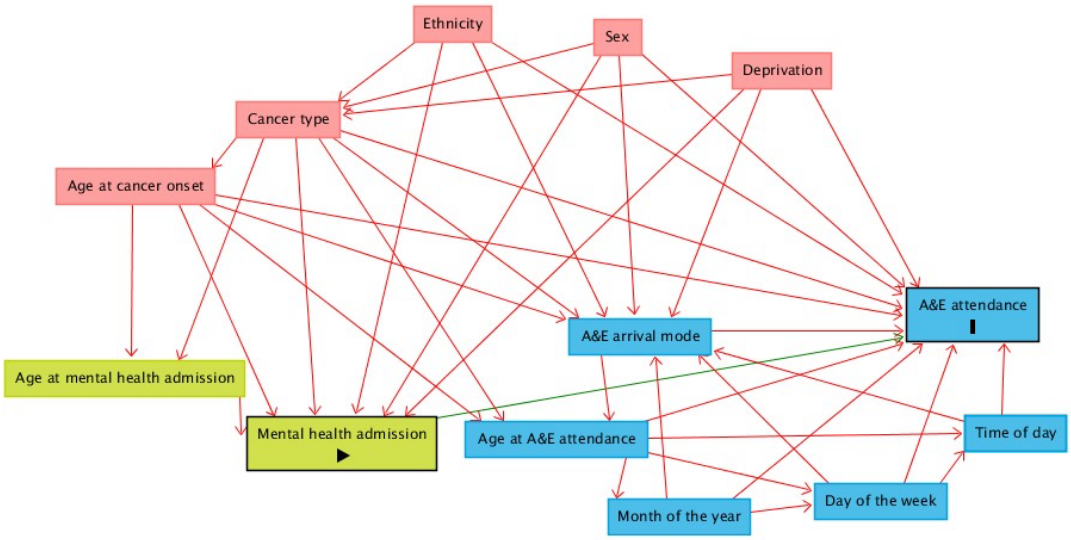
Figure F.13: A&E attendance - age at A&E attendance.



Confounders: ethnicity, sex, deprivation.

Mediators: Age at cancer onset, age at A&E attendance, A&E arrival mode, A&E attendance month, A&E attendance day of the week, A&E attendance time of day.

Figure F.14: A&E attendance - cancer type.

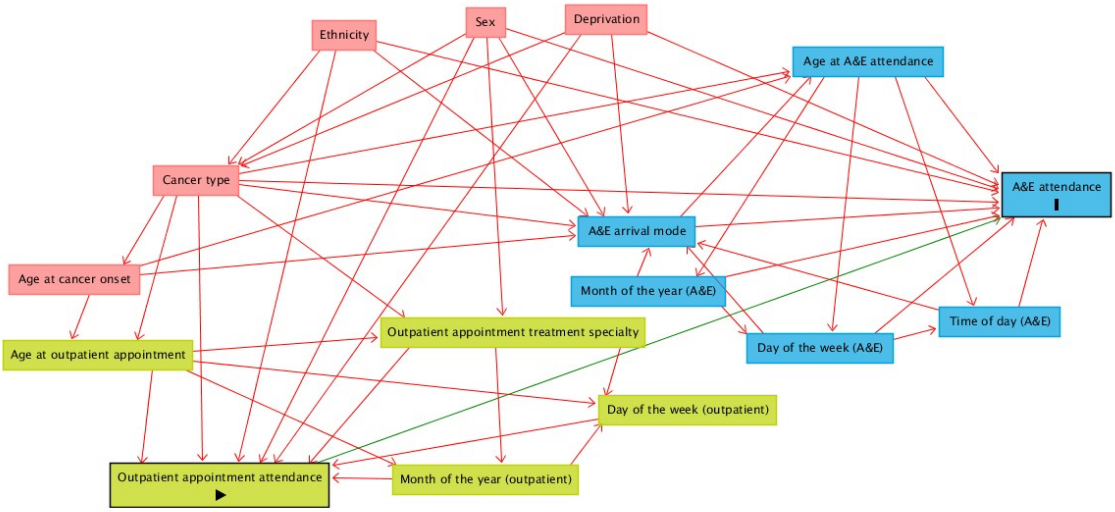


Confounders: ethnicity, sex, deprivation.

Proxy confounders: Age at cancer onset, cancer type, age at mental health admission.

Competing exposures: Age at A&E attendance, A&E arrival mode, A&E attendance month, A&E attendance day of the week, A&E attendance time of day.

Figure F.15: A&E attendance - mental health admission.



Confounders: ethnicity, sex, deprivation.

Proxy confounders: Age at cancer onset, cancer type, age at outpatient appointment, outpatient appointment treatment specialty, month of the year (outpatient), day of the week (outpatient).

Competing exposures: Age at A&E attendance, A&E arrival mode, A&E attendance month, A&E attendance day of the week, A&E attendance time of day.

Figure F.16: A&E attendance - outpatient appointment attendance.