University College London
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Understanding excess child and adolescent mortality in the United Kingdom compared with the EU15+ countries

A thesis submitted for the degree of Doctor of Philosophy

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Declaration

I, Joseph Ward, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Joseph Ward

Abstract

Background

Understanding why mortality in children and young people (CYP) in the UK is higher than similar high-income countries can inform efforts to improve outcomes.

Methods

I used data from the World Mortality Database, Office for National Statistics, and Global Burden of Disease Study to describe current patterns and long-term trends in UK CYP mortality, and compare this to a group of similar countries (the EU5+). I then used Hospital Episode Statistics data to understand how health service factors may contribute to the UK's poor outcomes, and identify patterns of healthcare activity associated with mortality hazard. I finally place concerns regarding UK adolescent mortality in an international context, and examine global trends in deaths in 10-24 year olds.

Results

I found large differences in rates of mortality decline in the UK by age group and cause, with adolescents lagging behind other age groups. Improvements in UK mortality since 1970 have also been slower than the EU15+. I found the UK to currently have significantly higher CYP mortality for respiratory conditions, neurological conditions, common infections, and diabetes and endocrine conditions, but good outcomes for injuries.

I found some areas of England to have mortality rates comparable with the best performing EU15+ countries, and that levels of deprivation explain much of the geographic variation in UK CYP mortality.

Amongst CYP admitted with epilepsy, asthma and diabetes, (conditions where the UK has high mortality), recurrent attendances to hospital, missed appointments, mental health contacts, and difficulties transitioning to adult services, were all associated with increased mortality hazard.

Global trends in adolescent mortality mirrored concerns in the UK, with poor progress compared with younger groups, despite most causes of death being preventable.

Conclusions

Interventions to improve UK CYP mortality require action across multiple health determinants. This should include addressing high levels of CYP poverty, but also further examination of the contribution of health service factors.

Impact Statement

Analyses in this thesis are likely to inform proposed initiatives to monitor UK child and young person (CYP) mortality by the Royal College of Paediatrics and Child Health (RCPCH) and other stakeholders. My findings regarding current CYP mortality differences between the UK and comparable high income countries (the EU15+), and likely future excess deaths if trends continue (Chapter 4), highlight the pressing need to intensify government and professional interest, further research, and charity involvement in this issue. This work has already contributed to the RCPCH's campaign to raise awareness of high UK CYP mortality, through publication of the RCPCH report C*hild health in 2030 in England: comparisons with other wealthy countries* (2018). I also presented these findings at a plenary session of the RCPCH conference in 2019, and published the analysis in *Archives of Disease in Childhood* in 2020.

My findings of specific causes where the UK has higher mortality than the EU15+ will have direct benefit for public health and clinical researchers specializing in these fields, highlighting where to target interventions to improve outcomes. Charities specializing in these causes will be able to use these results to advocate for improvements within services, and academics will be able to use these findings to support the case for research funding. My analysis of CYP mortality at local authority level (Chapters 5 and 6) will be of interest to both local and national government, in order to develop targeted initiatives where there is greatest excess mortality.

My analysis using Hospital Episode Statistics data illustrating sharp increases in emergency secondary care (Chapter 7), and opportunities to identify CYP at most risk of death (Chapter 8), contributed to the RCPCH *Paediatrics 2040 project* launched in 2021, which aimed to establish likely future changes needed to paediatric services in the UK. HES analyses included in this thesis may also be used to support the need for further health systems research to investigate the effectiveness of different ways of delivering services, in line with plans for more integrated models of care outlined in the NHS Long Term Plan (2019). Skills developed through this work have also enabled me to contribute to further projects using HES data, and collaborate on a successful National Institute of Health Research grant to explore direct and indirect impacts of the COVID-19 pandemic on CYP health, in partnership with NHS England.

My analysis of adolescent mortality in Chapter 9 will be of broad international interest, being the first systematic global study of mortality in young people for a decade. As recognition grows of the crucial role of young people to the sustainable development agenda, my findings will be of major interest to a broad range of stakeholders, and contribute to formulating global and country-level action required to improve young person health in the post COVID-19 world. This analysis has been submitted for publication to *the Lancet* in collaboration with the Institute of Health Metrics and Evaluation.

List of abbreviations

BAME	Black, Asian and Minority Ethnic
CAG	Confidential Advisory Group
CAME	Centre for Maternal and Child Enquiries
CAMHS	Child and Adolescent Mental Health Services
CDOP	Child Death Overview Panel
CEMCH	Confidential Enquiry into Maternal and Child Health
CHR-UK	Child Health Review UK
CORP	Clinical Outcome Review Programmes
CYP	Children and Young People
DALY	Disability Adjusted Life Years
DUBE	Diabetes/urological/blood/endocrine
EU	European Union
GBD	Global Burden of Disease
HES	Hospital Episode Statistics
HR	Hazard Ratio
ICD	International Classification of Diseases
IHME	Institute of Health Metrics and Evaluation
IMD	Index of Multiple Deprivation
IRR	Incident Rate Ratio
LSOA	Lower Super Output Area
MCCD	Medical Certificate of Causes of Death
NCB	National Children's Bureau
NCD	Non-Communicable Diseases
NCMD	National Child Mortality Database
NHS	National Health Service
NS-SEC	National Statistics Socioeconomic Classification
ONS	Office for National Statistics
RCPCH	Royal College of Paediatrics and Child Health
SDI	Sociodemographic Index
UK	United Kingdom
WHO	World Health Organization
WMD	World Mortality Database
YLL	Years of Life Lost

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List of publications related to this thesis

Ward JL, Wolfe I, Viner RM Cause-specific child and adolescent mortality in the UK and EU15+ countries *Arch Dis Child* 2020

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Introduction

Mortality is a fundamental indicator of population health and development which has been recorded since antiquity.[1] National trends in mortality reflect progress in addressing a broad range of economic and social determinants of health, and the effectiveness of health systems.[2,3] Deaths in children and young people (CYP) are considered a particularly sensitive marker of the health of populations, and tracking progress in CYP mortality is routinely included in national and multinational public health indicator sets.[4-7] Further, countries have both moral and legal responsibilities to protect CYP from harm and promote their wellbeing. Included within the United Nations Convention of the Rights of the Child is not only the right of every child to life, but also the obligation of nations to ensure to the maximum extent their survival.[8] Understanding the changing burden of CYP mortality, variation between populations, and identifying factors that may be contributing to poor outcomes, is essential for establishing if these responsibilities are being fulfilled, and to guide improvements.

There has been extraordinary progress in reducing mortality in CYP in the UK over the last 50 years, and deaths are now rare.[9] However, certain patterns and recent trends in CYP mortality reductions remain concerning. A high proportion of deaths that do occur are preventable, yet progress in reducing these has recently slowed.[10,11] Reductions in deaths have also not been evenly distributed by cause of death, age or socioeconomic group, and there is some evidence that inequalities in outcomes are increasing.[9] Of further concern are multiple analyses showing the UK to have higher CYP mortality than comparable high-income countries.[12-16] Viner et al. showed that although in 1970 the UK performed well compared to a group of countries with similar healthcare expenditures, slower rates of decline have eroded this position.[17] Subsequent studies have demonstrated continued poor outcomes for all-cause and non-communicable disease (NCD) mortality, particularly in younger children.[14,18] Comparisons with the best performing countries are particularly stark. In 2014 Wolfe et al. showed that reducing UK 0-14 mortality to the rate seen in Sweden would save 2000 lives a year,[13] and Zylbersztejn et al. recently estimated there to be around 600 extra deaths in 0-4

year olds from all causes in England compared with Sweden.[19] Worryingly, there is also evidence that the UK is set to fall further behind if current trends continue.[18]

Concern regarding current CYP mortality is widely acknowledged. Reducing UK CYP mortality was identified as a national priority by the Chief Medical Officer (CMO)[15] and the Department of Health Children and Young People's Health Outcomes Forum,[16] and as a key commitment in the UK Government's *"Better health outcomes for children and young people"* pledge.[20] Reducing excess mortality is also a central plank in planned work for CYP within NHS England's 10 year plan.[21] Yet explanations for the UK's poor mortality outcomes, needed to guide improvements, remain unclear.

Determinants of child and young person mortality

In order to make rational policy recommendations for CYP mortality we must consider the complex web of social and other determinants of mortality, how these vary between and within countries and over time, and the extent to which these factors are amenable to intervention.

The social determinants of health are defined by the World Health Organization (WHO) as "the conditions in which we are born, grow up, work and live."[22] Commonly used conceptual models to describe these include the "rainbow" schematic proposed by Dahlgren and Whitehead, incorporating the spectrum of individual (i.e. micro), meso and macro level determinants to health and survival.[23] Constitutional factors such as age and sex are placed at the centre within individual factors, then those relating to social and community networks, then living and working conditions, and finally general social, cultural and environmental conditions. Pearce et al. adapted this to describe social determinants relating to CYP, incorporating the importance of health patterns and behaviours in carers to CYP health, and factors relating to school, child care and family structure.[24]

Intersecting all these domains are socioeconomic factors relating to CYP health and survival.[25,26] Differences in CYP mortality by socioeconomic status have been described in multiple studies in high income countries for decades, with CYP from deprived backgrounds

more likely to die than their richer peers.[12,19,27-39] These differences are not limited to the most deprived groups, with health outcomes worsening with each unit increase in socioeconomic disadvantage, regardless of which metric is used.[24] Analyses have shown gradients in mortality to exist for both all causes and multiple specific causes of death in CYP including those due to cancer,[30-32] and external causes such as road traffic accidents, suicide, injury and poisoning.[33-36] Some analyses have shown associations with socioeconomic status and health outcomes to weaken in adolescence and early adulthood,[36] however the evidence for this is mixed, and variation in mortality by deprivation has been demonstrated across all CYP age groups.[29,36] We will discuss possible mechanisms through which socioeconomic status affects CYP mortality in greater detail in Chapter 6, but these include factors related to material deprivation, psychological pathways related to stress, structural factors, and effects of health behaviours and access to care. These factors interact with each level of determinants described by Dahlgren and Whitehead and others, and over time throughout the life-course.[24]

At the centre of Dahlgren and Whitehead's conceptual model are constitutional determinants: biological and psychological factors intrinsic to CYP, such as age, sex, ethnicity and factors related to birth. There are large differences in CYP mortality by sex.[25,40,41] Excess mortality amongst males compared with females is a consistent finding described across the early life course, from the perinatal period[42] to adolescence and young adulthood.[41] Explanations for these differences are complex and not fully understood. Among infants, possible explanations include greater resistance to infection in females and slower biological development in males.[40] In adolescence, sex differences are mainly the result of excess mortality due to self-harm, injury and violence in males.[41]

Differences in CYP mortality by ethnicity in the UK are also described, particularly amongst infants and younger children. The recent MBRRACE-UK Perinatal Surveillance report using data from 2018 found perinatal outcomes to be far worse amongst children from minority ethnic backgrounds, with around 50-60% higher neonatal mortality amongst children from Black or Asian ethnicity compared with White ethnicity, and similar trends seen in stillbirths.[43] Through examining variation in perinatal mortality over time by ethnicity, the report also concludes that current interventions to improve perinatal outcomes in the UK are currently

more impactful amongst children from White backgrounds.[43] Other studies have found higher overall mortality amongst CYP aged 28 days -17 years in families of Pakistani and Black African ethnicity compared with White ethnicity, but with no difference noted in Indian, Bangladeshi and black Caribbean CYP.[44] CYP from minority ethnic backgrounds have also been over-represented in non-accidental violent deaths.[44] More recent data show similar findings: although minority ethnic groups make up around 20% of the total population of CYP aged 0-24 in England and Wales, they contributed to almost 40% of all deaths reported to National Child Mortality Database (NCMD) in 2019,[45] and almost two thirds of deaths classified as homicide, according to data from ONS.[46] Explanations for these associations include complex interactions between socioeconomic factors, but also concerns around the impact of structural racism.[47-50]

Perinatal factors continue to contribute to mortality throughout the early life course. Mortality during childhood and adolescence remains higher amongst CYP with previous history of low birthweight and prematurity,[25,51] and prematurity increases risk of chronic illness and hospitalization.[51] The incidence and survival of children born pre-term is increasing in the UK and other high-income countries,[52] and the effect of this on national CYP mortality rates as a result of medical problems associated with prematurity, including rates of neuro-disability, may be considerable. It was previously estimated that around a third of CYP who die under the age of 18 in the UK have some form of neurodisability or developmental delay,[44] with up to 70% having some pre-existing chronic condition.[53] As with other determinants, perinatal factors related to CYP mortality are closely associated with family socioeconomic status.[54]

Health behaviours related to CYP mortality are also heavily patterned by socioeconomic factors and include alcohol, substance misuse, and risk taking behaviour in young people, as are effects of these factors on parents and carers of CYP.[13,41,55] For example, high rates of smoking during pregnancy amongst more deprived groups increases multiple perinatal risks, leading to subsequent higher mortality in later childhood.[56] Similarly, factors relating to the physical environment and CYP mortality, such as those relating to population density, the built environment, risk of injury inside and outside the home, road traffic safety and air pollution, are also heavily associated with deprivation. CYP from deprived backgrounds are

more likely to live in unsafe housing without access to safe areas to play, and there are steep social gradients in road traffic accidents and unintentional injury amongst 3-5 year olds and higher rates of emergency hospital admission following injuries in deprived groups.[57,58]

Factors relating to health service delivery in high income countries and CYP mortality are complex. Sidebotham et al. describes these as being related to either individual health practitioners, health-care services or national health policy.[25] At the level of individual healthcare practitioners, the failure to recognise serious acute illness is recurring factor to childhood deaths in the UK,[44,59,60] and delayed diagnosis of serious infection in children is a common theme in successful litigation cases against the NHS.[61] Adverse events resulting from individual medical error or system failures are also related to other determinants of CYP mortality, with CYP from deprived backgrounds and those with complex medical problems particularly susceptible.[45] Adequate training and supervision for healthcare professionals who look after CYP is an important factor to consider in preventing these deaths. However, these need to be viewed within the broader context of factors relating to health-care providers, how health services are organised and configured, and how adaptive they are for managing differing priorities for acute and chronic illnesses in CYP. Large differences in health-outcomes have been described between health-care providers operating with the same health system, including in the UK.[62-64] For example, variation in access to specialist tertiary paediatric neurology services between secondary health-care providers in England has been found to be associated CYP mortality due to epilepsy.[65] Understanding these differences, and identifying and learning from providers with the best outcomes, may aid improvements in other centres within the same system. There is also large variation in how healthcare systems are organised between high income countries, including barriers to accessing general practice and clinicians with expertise in paediatrics, and these may contribute to international mortality differences. The degree to which health services in the community and those in hospital settings are integrated is of particular interest, as the burden of illness in CYP continues to transition from predominantly acute communicable disease, (for which hospital-centric health service models were designed), to the needs of managing chronic non-communicable illness in CYP.[66] There is broad agreement this requires a shift in focus for health-service delivery, and introducing models of care which aim to transcend barriers between hospital and community services. Comparing primary and secondary care

integration with similar high-income countries may provide useful insights to adapting models of care for the UK.

At the macro level, the broader political and economic context in which health services operate is fundamental to understanding how health service factors affect CYP mortality. These include factors related to health policy and how health services are funded, but also the provision of social care, education and welfare systems, and the extent to which child-centric policies across all areas of government are prioritised. These decisions will have impacts within health services factors, but also across the multiple other determinants of CYP mortality described above.[25]

Understanding patterns in UK child and young person mortality

Previous work has sought to describe patterns of UK CYP mortality, and has identified common themes relating to determinants described above which may be contributing to poor outcomes in the UK. These broadly stem from either the system of national Confidential Enquiries, through reviewing individual child deaths or using routine vital statistics to describe variation in outcomes at population level.

National confidential enquiries and child and young person mortality

The system of confidential enquiries in the UK seeks to apply a standard methodology to understand patterns of mortality and morbidity in order to guide improvements. The basic functions of a confidential enquiry are to maintain a register of the cases under review, and subject cases (or a sample of them) to an expert review panel tasked with identifying avoidable factors related to adverse outcomes.[59] Although CYP have been included in previous confidential enquiries,[67-73] it was not until the formation of the Confidential Enquiry into Maternal and Child Health (CEMACH) in 2003 where a systematic approach to reviewing deaths in CYP from infancy to 18 years of age was attempted.[59,67] In 2008 CEMACH published the first report of a national confidential enquiry specifically focused on deaths in CYP.[59] The main objectives were: to identify all deaths occurring in 2006 in CYP aged 28 days to 17 years and 364 days in Wales, Northern Ireland and three regions of England (South West, North East & West Midlands); collect a core dataset on all those deaths; conduct a detailed review

of a subset of these deaths to identify avoidable factors; inform feasibility of conducting national confidential enquiry work into child deaths.[59] The study covered around a third of the UK population aged 0-18, identifying 957 deaths. Population level findings highlighted large differences in mortality by gender in adolescents, but not young children. Regional variation in deaths were also identified, with worse outcomes in Northern Ireland and North East England, predominantly due to excess injury mortality and self-harm. The findings also demonstrated the growing contribution to total mortality of CYP with complex medical problems, steep social gradients in CYP mortality, with worse outcomes amongst more deprived children, and differences by ethnicity.[59]

CEMACH then selected a sample from this core dataset for case review to identify avoidable factors antecedent to death. 124 cases (12%) were selected, broadly reflecting the age, sex and regional distribution of deaths in the core dataset. Of these 119 had data available to ascertain if there were avoidable factors at the individual level. The report defined "avoidable" deaths as those where either direct or indirect failures in care were identified by any agency with responsibilty for the child or young person (including the parents). Using these definitions, avoidable factors were identified in 26% (31 of 119 cases) and potentially avoidable factors in 43% of cases reviewed.[59] The main themes identified included the failure to recognise severe illness, examine or interpret clinical signs, understand the importance of clinical history, delays in referral, and poor inter-agency communication. The panels found these were often compounded by the assessment being performed by individuals lacking experience in paediatric care who were not supervised sufficiently. Missed appointments, particularly in the context of a referral to Child and Adolescent Mental Health Services (CAMHS), were also highlighted as a source of concern.[59] The authors then conducted an analysis on a subset of 154 deaths occurring in the North East of England to assess contact with primary care prior to death. Amongst cases where the GP was involved in the management of the condition which led to death, the authors found avoidable factors in around a quarter of cases, and potentially avoidable factors in a further quarter. Particular concerns were identified regarding the care of CYP with chronic illnesses such as asthma and epilepsy.[59] Harnden et al then conducted an independent review of primary care within the main Confidential Enquiry, identifying primary care records for 168 children aged 28 days – 17 years. Avoidable primary care factors were identified in 20% of cases, and included the

failure to recognise serious infections in CYP, and further concern around inadequate management of epilepsy and asthma.[60]

Population level trends in UK child and young person mortality

In 2009 CEMACH was renamed the Centre for Maternal and Child Enquiries (CAME) and in 2010 all confidential enquiries were replaced within newly established Clinical Outcome Review Programmes (CORP).[74,75] Surveillance of maternal and perinatal outcomes was separated from that for older children,[74] with the child health aspects of the CORP run by the Royal College of Paediatrics and Child Health (RCPCH) within Child Health Review UK (CHR-UK). In 2013 CHR-UK published *Overview of child deaths in the four UK countries*,[53] and a further report focusing on deaths due to epilepsy.[76] Adopting a different approach to CEMACH, *Overview of child deaths in the four UK countries* used routinely collected statistics and hospitalisation data to describe trends in UK mortality in 1-18 year olds from 1980 – 2013. As found in CEMACH, the authors note wide variation in CYP mortality between the countries of the UK, with outcomes in England and Wales better than in Northern Ireland and Scotland. Recommendations to reduce deaths included focusing on the leading causes of death where progress has been slow, such as intentional injury, and on the increasing importance of chronic diseases to total mortality burden.[53] The RCPCH reports *Why Children Di*e 2014[13], and *State of Child Health* series, first published in 2017[12] and updated periodically[55,77] have also used routinely available mortality data to describe UK CYP mortality. These have also highlighted the growing contribution of chronic diseases to CYP mortality, key differences in outcomes between the countries of the UK, steep social gradients in outcomes within the UK. These reports were also some of the first to raise concerns regarding UK CYP mortality performance compared with other similar countries.

Reviews of individual child deaths and establishing the National Child Mortality Database

Reviews of individual deaths have long contributed to understanding CYP mortality trends in the UK and informed strategies aiming to improve outcomes. Although these have primarily focused on cases where abuse or neglect are suspected,[78,79] these have also included concerns around the care of CYP prior to other causes of death.[80] Dating from 1940s, these

reviews have had a substantial impact on national guidance and legislation,[78,79] but their impact on preventing future deaths is unclear.

Notable reviews of individual cases include the Inquiry into the death of Victoria Climbié in 2003,[81] which led to wholesale reform of national guidance to identify and safeguard vulnerable children. Following the inquiry the government set out a process to individually review all child deaths in England with the publication of Working Together to Safeguard Children in 2006.[82] As a result, a system to review the circumstances around every death in childhood, and identify potentially modifiable factors, was introduced in 2008, with every local authority required to establish Child Death Overview Panels (CDOP) under the responsibility of Local Safeguarding Children's Boards (LCSB). These data can provide valuable context to deaths in CYP from multiple professionals, and identify avoidable factors in around a third of deaths reviewed.[11] However, significant variation in how the CDOP process operates within the 152 LSCBs in England present multiple barriers to collate these data to inform interventions at the national level.[83] There are real opportunities for these data to be used in future analyses however, through efforts to standardize this process and improve the quality and completeness of data collected with the formation of the National Child Mortality Database (NCMD) in 2019.[83]

Explanations for UK child and young person mortality differences

Analyses described above have identified common themes in UK CYP deaths which may explain differences internationally and warrant further study. For example, higher levels of child poverty than the best performing countries for CYP mortality likely contribute to the UK's poor performance,[84-87] with steep social gradients in outcomes highlighted by the RCPCH,[77] CEMACH and elsewhere.[19] However, there has not been a systematic exploration of the impact of poverty or inequality on specific NCD causes/disorders where UK has excess mortality. Further, observing the association between child poverty and mortality does not explain the multiple mechanisms through which it is operating, or how poverty interacts with health service utilization and provision. There is evidence that poverty is associated with how CYP access and use health services.[88,89] How responsive the health service is to additional

needs of CYP from deprived backgrounds may contribute to increased mortality for certain conditions.

As identified in the CEMACH and RCPCH work, exploring geographic variation across the UK for CYP mortality will also aid understanding of the UK's performance as a whole.[44,62] Although regional differences may represent variability in social determinants, as hospital care for common paediatric NCDs differs greatly by region[62] this may also reflect modifiable healthcare amenable factors. Understanding patterns of healthcare use in CYP who subsequently die of conditions where UK mortality is high may also provide insights in to identifying where additional support is needed. However, a systematic analysis of the contribution of healthcare factors on CYP mortality, and how these vary by region and socioeconomic status, is lacking.

Project plan

This thesis will seek to explore factors which may be contributing to high CYP mortality in the UK. Guided by previous work describing patterns and concerns in CYP mortality in the UK and the determinants of mortality described above, I will: investigate current and forecasted burden of CYP mortality in the UK compared with other high-income countries, explore geographic, socioeconomic and demographic variation in outcomes, and investigate how patterns in healthcare utilization may be used to identify CYP at greatest risk of death. As the UK's poor perinatal and neonatal outcomes are well described,[19,90-93] this thesis will focus on CYP aged 1-24. Extending the age bracket to 24 both ensures this analysis captures the full social, biological and neurocognitive transitions that occur during adolescence,[94] and reflects plans to move towards a "0-25" service model by 2028 within England outlined in the NHS long term plan.[21]

In Chapter 1 I will describe a literature review of previous studies comparing UK CYP mortality internationally. I will then describe the data and summarise the methods I will use to analyse CYP mortality in the UK in Chapter 2, including details of the process of death registration data and the reliability of mortality statistics, and involvement of CYP in the design of this thesis. In Chapter 3 I will describe the current burden of CYP mortality and compare trends

over time between age groups and by cause of death. In Chapter 4 I will analyse these trends relative to a group of similar high income countries (the EU15+), to identify the causes and age groups where there are currently excess UK CYP deaths, and use forecast data to describe predicted trends from 2016-2040. I will then investigate geographic, demographic and socioeconomic variation in CYP mortality within the UK in Chapter 5 and 6, identifying how these factors contribute to the UK's poor performance, and highlight where there is the greatest potential for improvement. In Chapter 7 and 8 I will explore patterns of healthcare utilisation prior to death for conditions identified as having excess UK mortality compared with EU15+ countries. Exploring how secondary health services are used in the years prior to death within these groups will potentially offer mechanisms to identify CYP who have high mortality risk and are in need of additional support. Finally, as Chapter 4 demonstrates deaths during adolescence appear to contribute to the UKs poor performance,[95] and Chapters 5 and 6 show this age group has some of the widest geographic and socioeconomic variations in UK mortality, I will examine UK outcomes in this age group in the global context, and describe international trends in mortality amongst 10-24 in Chapter 9.

Research aim:

1. Explore potential reasons that UK child and adolescent mortality is higher than many/most other similar wealthy nations to inform strategies for improvement

Research objectives:

1. Describe current burden of mortality in the UK and recent trends in mortality in 1-24 year olds
2. Identify groups of causes of death where there is excess child and adolescent mortality in the UK, compared to the EU15+
3. Understand demographic, socioeconomic and regional variation in child and young person mortality across the UK
4. Assess the contribution of health system factors to predominant causes of child and adolescent mortality in the UK.
5. Describe trends in UK adolescent mortality in its global context.

Chapter 1

Literature review of studies comparing UK child and young person mortality internationally

In order to explore concern regarding high child and young person (CYP) mortality in the UK, and identify gaps in the literature, it is necessary to first systematically describe existing evidence that UK outcomes may be worse than in comparable wealthy countries.

I conducted a systematic review to identify studies comparing UK CYP (1-24) mortality with other high-income countries. I searched PubMed for studies published between 1st September 2008 to 1st September 2018 using the following terms in titles or abstracts: United Kingdom OR UK OR England OR Wales OR Scotland OR Northern Ireland AND death OR deaths OR mortality AND child OR children OR adolescent OR youth OR young people, and then checked reference lists for further papers. I limited the search to studies published within the last 10 years (2008 – 2018) as the research objective is to understand recent poor performance in UK outcomes. The search was updated on 20th March 2020, (and one additional study identified). The inclusion and exclusion criteria are shown in table 1.

Table 1: Inclusion and exclusion criteria for literature review

Inclusion criteria
Child and young person (1-24) mortality from any cause
Population level mortality in the UK (or constituent countries)
Comparison of UK outcomes with population level mortality in any high-income country*
Published 1st Sept 2008 – 20th March 2020
Exclusion criteria
Regional level mortality
Comparison not UK focused

*as defined by the World Bank in 2018

Assessing the quality of included studies

I used the Quality Assessment Tool provided by the National Heart, Lung and Blood Institute to assess the quality of the cohort studies identified.[96] There is currently no agreed validated assessment tool for ecological studies, although plans to extend STROBE guidance for this purpose has been proposed.[97] Others have noted that future STROBE guidance is likely to include items to assess the quality and relevance of ecological studies proposed by Dufault et al,[98,99] and these have been adapted for use in other systematic reviews.[100,101] Here I use an assessment tool developed by Cortes-Ramirez et al.[100] based on the Dufault et al[98] proposal and described in table 2 (p.44). These studies had a maximum score of 12 points, and were defined as: low relevance (<5 points), medium relevance (5-8 points) and high relevance (>8 points).

Literature review results

Figure 1 (p.43) shows the PRISMA flowchart of studies included in the review. I reviewed the title/abstracts of 1277 studies, and identified 17 studies where population level UK CYP mortality outcomes (1-24) were compared with other high-income countries, shown in table 3 (p.45). Of these, 4 were cohort studies, of which two were birth cohorts,[19,102] and two were cohorts of national cancer registries.[103,104] All of the cohort studies were rated as "good". The remaining 13 studies were ecological studies,[14,17,105-115] of which 6 were rated as "high relevance" and 7 as "medium relevance" (tables 4 and 5 p.48).

Four studies examined differences in all-cause or total NCD mortality. Using data to 2010, Wolfe et al. showed that reducing UK 0-14 mortality to the rate seen in Sweden would save 2000 lives a year, or 5 a day.[108] Zylbersztejn et al. recently estimated there to be around 600 extra deaths 2 days-4 years from all causes in England compared with Sweden.[19] Viner and Wolfe showed the UK to continue to fall behind comparable wealthy nations for mortality from all causes and total NCD mortality using data to 2010[14] and 2014[105]

The only systematic investigation identified of grouped cause mortality in 1-24 year olds was Viner et al's 2014 study using data to 2008.[17] The authors showed that whereas in 1970 the

UK performed well compared to a group of similar high income countries, by 2008 slower declines in mortality have resulted in an estimated 1000 excess deaths in children and infants, and around 280 excess deaths amongst 10-24 year olds from NCDs, each year.[17] Cause specific analyses found the UK to have higher CYP mortality for endocrine, respiratory, digestive, and particularly neuropsychiatric causes (epilepsy, cerebral palsy and substance misuse).[17] Tambe et al used ICD10 code chapter heading to compare mortality in 0-4 year olds[107] and 5-15 year olds[106] (but not older adolescents) in the UK and Sweden between 2006 and 2008. They found higher all cause mortality in the UK in both age groups in addition to worse outcomes for diseases of the respiratory system, infections (respiratory infections and septicaemia), diseases of the circulatory system, gastroentestinal conditions, nervous system, neoplasms and neonatal conditions.

Eleven studies examined outcomes from specific causes of death. Zylbersztejn et al. found mortality rates due to respiratory infections amongst 1-4 year olds to be around 30% higher in England compared with Sweden, after adjusting for differences in birth characteristics and socioeconomic factors, using data from 2003 – 2012.[102] Wolfe et al. showed the UK to have higher 0-14 year old mortality from meningococcal disease, pneumonia and asthma compared with other European countries using data from 2000-2010.[108,110] Chatenoud et al. also found the UK to perform poorly for asthma mortality in CYP, and to have slower rates of decline between 1994 -2004, compared with four other European countries.[111] I identified two studies comparing cancer survival in the UK internationally. Mathew et al compared survival from the most common malignant paediatric (under 15) CNS tumours in the UK with the US between 1996 and 2005.[104] Overall age adjusted survival was significantly lower in the UK at 1, 5, and 10 years post histological diagnosis. Similarly, Pritchard-Jones et al. showed worse survival in the UK from Wilms tumour, and delay in diagnosis, in a recent analysis comparing outcomes with Germany.[103]

Two studies looked specifically at injury mortality. Polinder et al.[112] identified the UK to have one of the lowest mortality for intentional and unintentional injuries in 0-24 year olds of 8 rich countries examined in 2005. Anhgari et al.[113] showed the UK to be the best performing country for road traffic mortality in children 0-14 compared with 15 high income countries, and to also perform well for adolescent and young adult injury mortality. Viner et al. also

found UK injury mortality to be lower than the EU15+ average in all age groups using data to 2008[17] and to 2014.[18] Parts of the UK were also identified to have lower suicide mortality compared with comparable countries. Värnik et al showed suicide mortality in England in 15-24 year olds to be one of the lowest among 15 European countries using data between 2000-2004/5.[114] Murphy et al. also showed the Republic of Ireland to have higher suicide mortality in young adults than England and Wales in their analysis of trends 1980 – 2010, but to have similar outcomes to Northern Ireland and Scotland.[115]

Additional studies and reports

The CONCORD[116], EUROCARE[117] and Automated Childhood Cancer Information System (ACCIS)[118,119] projects publish population based cancer incidence and survival estimates which include children and adolescents, although these do not focus on comparing UK CYP outcomes internationally. EUROCARE 5 show survival data from 2000 – 2007 from 29 countries, and provides some evidence that total UK cancer survival may be lower than parts of Europe.[117] The latest iteration of the CONCORD programme (CONCORD-3) compares survival 2000–2014 of three malignancies in children 0-14 within 71 countries. The UK is shown to have one of the highest rates of 5-year survival for acute lymphoblastic leukaemia and lymphoma. Although the authors highlight the difficulties of comparing brain tumour outcomes internationally, due to differences in diagnosis, classification and registration practices, they report some evidence that UK survival may be slightly lower than the best performing countries.[116]

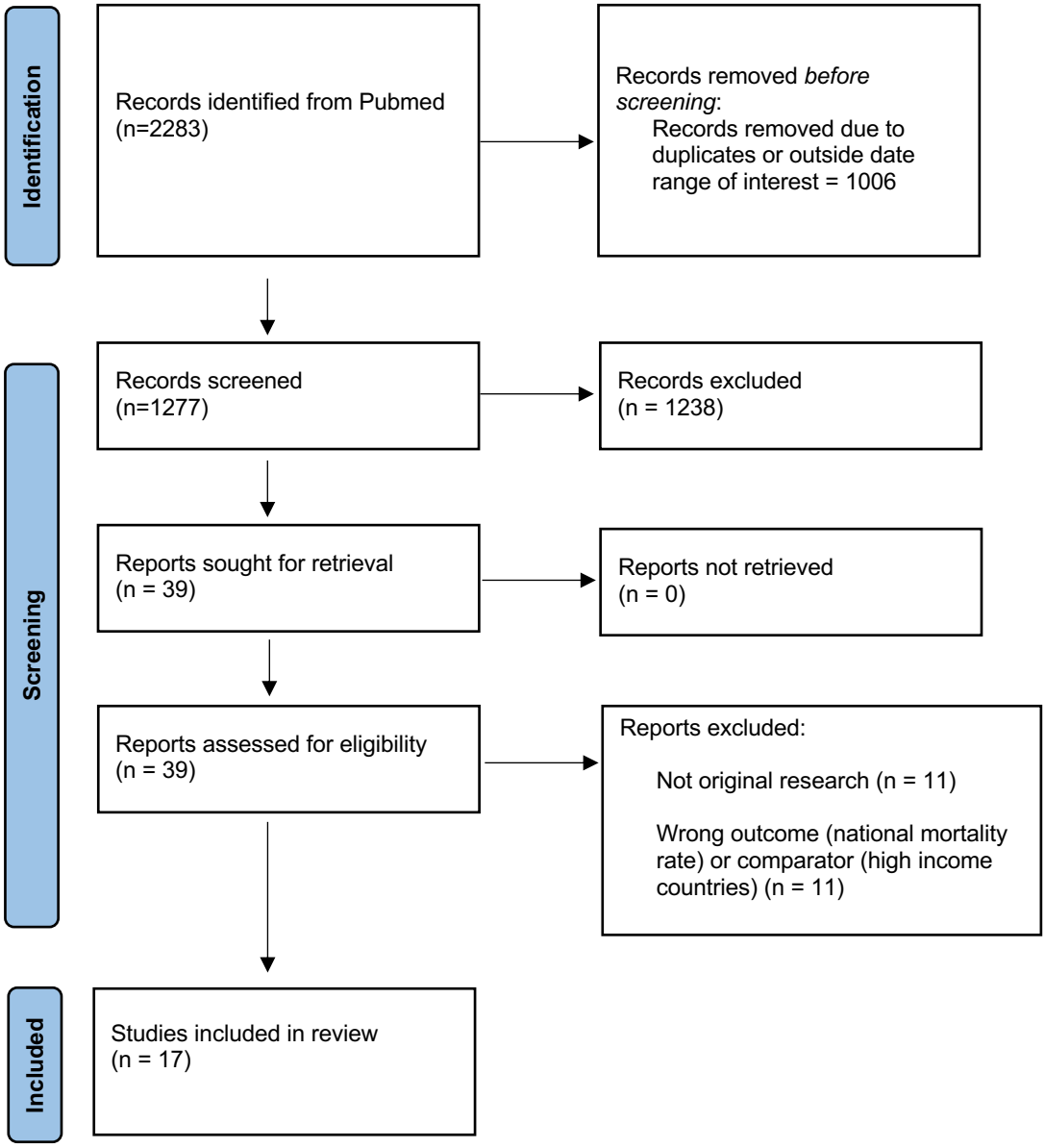
Multiple international bodies (e.g. UNICEF, OECD, WHO, European Union) produce descriptive reports of national CYP mortality estimates by geographical region. Similarly, the Global Burden of Disease study produces periodic national cause specific mortality estimates for almost all countries and territories of the world.[120] Although these are informative to highlight the UK's position, as they do not focus on analysing UK CYP outcomes compared with other high-income countries, they were not included in this review.

Literature review summary

In this literature review I identified multiple studies showing UK CYP mortality outcomes to be worse than comparable wealthy countries for all-cause, some infectious diseases and a broad range of NCDs, with injury and suicide mortality found to be lower in the UK. However, this also demonstrated an important evidence gap: the most recent systematic international comparison of UK all-cause mortality to include CYP 1-24 used data only to 2008, and recent studies identifying cause specific differences in CYP mortality in the UK with comparable countries are also lacking.

In Chapter 4 I address this, and analyse UK CYP mortality trends between 1970 – 2016 in 1-24 compared with a group of high income countries (the EU15+), assess current differences in mortality by cause of death, and use forecast data to estimate future excess deaths in the UK if current trends continue. I then go on to explore regional, socioeconomic and demographic variation in UK CYP mortality in detail (Chapter 5 and 6), before considering healthcare service use amongst CYP admitted to hospital with conditions where UK mortality is high (Chapter 7 and 8).

Figure 1: PRISMA Flowchart for included studies in systematic review adapted from Page, McKenzie, Bossuyt et al.[121]



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Table 2: Assessment of ecological studies adapted from Dufault and Klar[98]

	Item	Description
Study design and focus	Sample size (max = 2)	Number of ecologic units included in the analysis as a proportion of the total number of units (3 levels: < 11% = 0 points; 11-79% = 1 point; > 79% = 2 points)
	Level of inference (max = 1)	The results of the analysis are not used to draw inferences for individuals
	Pre-specification of ecological units (max = 1)	Ecological units are selected to suit the hypothesis (as opposed to seemingly motivated by convenience or necessity such as the use of districts, towns or counties)
Statistical methodology (max = 5)	Validity of statistical inferences (max = 2)	Number of ecological units per covariate (3 levels: 0-10 = 0 points; 10-20 = 1 point; > 20 = 2 points)
	Use of covariates (max = 1)	Analysis adjusted for covariates (e.g. sociodemographic; environmental risk factors)
	Proper adjustment for covariates (max = 1)	Covariates are properly adjusted when regressed upon adjusted outcomes as recommended for ecological studies
	Spatial effects (max = 1)	Inclusion of spatial analysis
Quality of reporting (max = 3)	Statement of study design (max = 1)	Key elements of the study design are presented in the report
	Justification of study design (max = 1)	Justification of the ecological analysis, the rationale and the objectives are presented in the report
	Discussion of cross-level bias and limitations (max = 1)	Readers are cautioned about the limitations of the ecological design and/or the ecological fallacy

Table 3: Summary of studies identified comparing UK CYP mortality with other high-income countries

	Age Group	Data date	Comparator	Cause of death	Main findings
Grouped / all causes					
Viner et al. 2018[105]	0-19 years	1970 - 2014	EU15+[i]	All cause, GBD[ii] category	NCD[iii] mortality higher than the EU15+ median. 1-4 all-cause mortality could be 140% of EU15+ median by 2030 if current trends continue
Zylbersztejn et al. 2018[19]	2 days – 4 years	2003 - 2012	Sweden	All cause	Higher all-cause mortality, explained by birth characteristics and socioeconomic factors
Tambe et al. 2016[106]	5-15 years	2006 - 2008	Sweden	ICD10 Chapter	Higher mortality in the UK for all causes, diseases of the respiratory system, infections, circulatory system, nervous system
Tambe et al. 2015[107]	0-5 years	2006-2008	Sweden	ICD10 Chapter	Higher UK mortality for all causes, respiratory conditions, cardiovascular conditions, infections, neurological conditions, neonatal disorders
Wolfe et al. 2015[14]	0-19 years	1970 - 2010	EU15+	All causes, GBD category	UK mortality quartile has worsened in all age groups since 1970. UK infant mortality was in the 90th centile of EU15+ countries in 2012, 75th centile for 1-4 year olds. Higher NCD mortality in 10-19 year olds than the median EU15+.
Viner et al. 2014[17]	0-24 years	1970 - 2008	EU15+	All causes, GBD category and ICD10 chapter	Slower mortality reductions for all age groups in the UK. All-cause mortality for children 1-4 in the worst quartile in 2008. NCD mortality in the worst quartile for all age groups. Higher UK mortality for endocrine, respiratory, digestive and neuropsychiatric causes. Injury mortality was in the best quartile for all age groups.
Wolfe et al. 2013[108]	0-14 years	2000 - 2010	EU15[iv]	All cause, pneumonia, asthma	If UK all-cause mortality were similar to Sweden, 1951 fewer deaths each year. UK had increased mortality for pneumonia and asthma

	Age Group	Data date	Comparator	Cause of death	Main findings
Pritchard et al. 2011[109]	0-14 years	1979 - 2005	20 high income countries	All-cause	UK had 5th highest all-cause mortality, but significantly greater rate of reduction than the US
Wolfe et al. 2011[110]	0-14 years	2003 - 2007	12 European countries	All-cause, meningococcal disease, pneumonia, asthma	Higher mortality in the UK than many European countries for causes examined
Specific causes					
Zylbersztejn et al 2020[102]	31 days – 5 years	2003 - 2012	Sweden	Respiratory tract infections	Mortality due to respiratory infections amongst 1-4 year olds 30% higher in England compared with Sweden, after adjusting for birth characteristics and socioeconomic status
Pritchard-Jones et Al. 2015[103]	Mean age 3 years	2002 - 2011	Germany	Wilms' tumour	Lower event free and overall 5-year survival in the UK
Chatenoud et al. 2009[111]	5-34 years	1994 - 2004	5 European countries	Deaths due to asthma	Third highest rate of deaths for asthma and slower rates of decline in young men in the UK
Mathew et al. 2014[104]	0-15 years	1996 - 2005	US	Paediatric CNS tumour survival	Lower survival in the UK at 1,5 and 10 years
Polinder et al. 2010[112]	0-24 years	2005	7 European Countries	Deaths due to injuries	UK and Netherlands identified as having the lowest injury mortality of all countries examined.
Ahangari et al. 2016[113]	0-24 years	1990 - 2010	15 high income countries	Road traffic fatalities	UK the best performing country for children 0-14 and had the highest rate of improvement. UK ranked in the best 6 countries for adolescent and young adult road traffic mortality.

	Age Group	Data date	Comparator	Cause of death	Main findings
Värnik et al. 2009[114]	15-24 years	2000 – 2004/5	15 European countries	Deaths due to suicide	England identified as having some of the lowest rates for suicide in both sexes.
Murphy et al. 2015[115]	15-24 years	1980 - 2010	Rep. Ireland	Deaths due to suicide	Lower suicide mortality in England and Wales compared with the Republic of Ireland. Rates in Scotland and Northern Ireland were similar to Republic of Ireland.

[i]EU15+: European Union countries pre-2004 plus Norway, Australia and Canada; [ii]GBD: Global Burden of Disease; [iii]NCD: Non–communicable disease; [iv]EU15: European Union countries pre-2004

Table 4: Assessment of quality of included cohort studies using the Assessment Tool for Observational Cohort Studies and Cross Sectional Studies provided by the National Heart, Lung and Blood Institute[96]

	Zylbersztejn et al. 2018[19]	Zylbersztejn et al 2020[102]	Pritchard-Jones et Al. 2015[103]	Mathew et al. 2014[104]
Was the research question or objective in this paper clearly stated?	Yes	Yes	Yes	Yes
Was the study population clearly specified and defined?	Yes	Yes	Yes	Yes
Was the participation rate of eligible persons at least 50%?	Yes	Yes	Yes	Yes
Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?	Yes	Yes	Yes	Yes
Was a sample size justification, power description, or variance and effect estimates provided?	No	No	No	No
For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?	Yes	Yes	Yes	Yes
Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?	Yes	Yes	Yes	Yes
For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?	N/A	N/A	N/A	N/A
Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	No	No	Yes	Yes
Was the exposure(s) assessed more than once over time?	No	No	No	No
Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?	Yes	Yes	Yes	Yes
Were the outcome assessors blinded to the exposure status of participants?	No	No	No	No
Was loss to follow-up after baseline 20% or less?	Yes	Yes	Yes	Yes
Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?	Yes	Yes	No	Yes

Table 5: Assessment of relevance of included ecological studies using Dufault and Klar criteria[98]

	Measure	Viner et al. 2018[9]	Tambe et al. 2016[12]	Tambe et al. 2015[11]	Wolfe et al. 2015[8]	Viner et al. 2014[10]	Wolfe et al. 2013[6]	Pritchard et al. 2011[27]	Wolfe et al. 2011[13]	Chatenoud et al. 2009[14]	Polinder et al. 2010[17]	Ahangari et al. 2016[18]	Värnik et al. 2009[20]	Murphy et al. 2015[21]
Study design	Sample size	2	2	2	2	2	2	2	2	2	2	2	2	2
	Level of inference	1	1	1	1	1	1	1	1	1	1	1	1	1
	Pre-specification of ecological units	1	1	1	1	1	1	0	1	1	1	1	1	1
Statistical methodology	Validity of statistical inferences	1	0	0	1	1	1	0	1	0	0	1	1	0
	Use of covariates	1	0	0	1	1	1	0	0	0	0	0	1	0
	Proper adjustment for covariates	1	0	0	1	1	1	0	0	0	0	0	0	0
	Spatial effects	0	0	0	0	0	0	0	0	0	0	0	0	0
Quality of reporting	Statement of study design	1	1	1	1	1	1	1	1	1	1	1	1	1
	Justification of study design	1	1	1	1	1	1	1	1	1	1	1	1	1
	Discussion of cross level bias and limitations	1	1	1	0	1	1	1	1	1	1	0	1	1
Score		10	7	7	9	10	10	6	8	7	7	7	9	7

Chapter 2

Data, methods and ethical approval

I use three groups of data to analyse UK CYP mortality in this thesis: mortality data from death registration from the Office for National Statistics (ONS) and World Health Organization (WHO), modelled data from the Global Burden of Disease study (GBD), and routine administrative data from Hospital Episode Statistics (HES). In this chapter I will summarise these datasets, describing how the strengths of each allow for a comprehensive analysis of UK CYP mortality. I then provide further methodological details relating to each analysis, the statistical methods used, procedures to clean data, group causes of death, and the strengths and limitations of these, within each chapter.

I first consider mortality datasets provided by ONS and the WHO included in this thesis. In order to assess the reliability and quality of these estimates, we must first consider the process of death registration. Here I describe how systems of death registration in the UK were established, and how shortcomings and practical considerations in these processes may affect national mortality estimates for CYP. The focus here will be on legislation related to England and Wales, but with key differences in Scotland and Northern Ireland also highlighted.

I then consider mortality estimates provided by the GBD study. These data are based on death registration where available, but are also modelled using multiple other sources to provide estimates where data are lacking. I describe how the study has evolved, and the main considerations in interpreting these data. Finally, I provide details of the administrative data used in this thesis within HES. HES data allow population level analyses of healthcare activity, but are subject to multiple limitations regarding data quality, cleaning procedures, and the data fields which are available. Use of these data for research purposes also presents unique ethical challenges, as they are collected without consent. As part of the approval process to gain access to HES data, I presented the analysis plan to CYP as part of a patient and public engagement initiative in order to understand these considerations and inform the application, which I also describe in this chapter. I finally provide details for the overall ethics

application and approvals for this thesis. Much of the data I use in this thesis are publicly available, however I will describe details regarding data access and permissions where relevant.

Death registration and mortality data

The history and evolution of death registration in the UK

Death registration in England and Wales has its origins in the Act for Registering Births, Deaths and Marriages in 1837, which provided the foundation for the collection of national vital statistics.[122] The Act introduced a civil, rather than ecclesiastical, system for death registration; prior its introduction, deaths, births and marriages registered outside of the Church of England did not have the same legal protection, and were not admissible as evidence in court.[123] Developing a national registration system was therefore as much related to social and legal reform, and the separation of the powers of State and Church, as to its importance to public health and population monitoring.

The Act established the General Register Office, headed by the Registrar General, which has since been charged with the collection and publication of mortality information in England and Wales. Following The Births and Deaths Registration Act 1874, death registration has been compulsory, and requires a medical practitioner who attended the deceased to provide a statement as to the cause of death, unless an inquest is held.[124] Further important revisions to the legal framework of death registration include The Births and Registration Act 1926, which introduced the standard death certificate, and required the certifier to provide a sequence of events that led to death, which is still required today.[124] Similar legislation introducing compulsory death registration was introduced in Scotland with the Registrations Act (1854)[125] and in Ireland following the Registration (Ireland, Births and Deaths) Act (1863).[126]

The process of death registration, underlying cause of death and the International Classification of Diseases

Most deaths are certified by a medical practitioner using the Medical Certificate of Causes of Death (MCCD).[127] In England and Wales, in order to complete the MCCD, the certifying medical practitioner must have seen the deceased within the last two weeks. The MCCD is then taken to the Registrar by an informant (usually a relative), within 5 days of death (8 days in Scotland).[127] In 2018, around 82.1% of all deaths were registered in this way in England and Wales.[128]

The MCCD comprises of two parts. Part 1 defines the sequences of events that led to death, and Part 2 the details of associated conditions that contributed to death, but are not part of the causal sequence. The underlying cause of death is defined by the WHO as "*the disease or injury that initiated the train of events directly leading to death"* or *"the circumstances of the accident or violence which produced the fatal injury*".[129] Deaths due to violence, accidents or poisonings are defined by the underlying cause from a list of external causes and then by the nature of the injury.[127]

The current system of classifying causes of death has its origins in the mid-19th century, with the medical statistician William Farr proposing the general arrangement of diseases by anatomical site in 1855. This provided the basis for the International List of Causes of Death, and then International Classification of Diseases (ICD), adopted in 1900.[124] The World Health Organization has published the subsequent iterations of the ICD since its inception in 1948. Although WHO Nomenclature Regulations adopted in 1967 require member states to use the most current edition of the ICD when reporting mortality statistics,[130] there is a marked time delay in countries adopting these, often hindering international comparisons of mortality. For example, ICD10 has been available for use since 1994, with the UK only adopting it in 2001, and Greece only doing so in 2014. ICD-11 is currently in process, and WHO member states will be able to start reporting deaths using this system in 2022.[131]

Death registration accuracy and reliability, and death certification reform

Studies have consistently found completion of the MCCD to be poor, with a high proportion having illogical or inappropriate causes of death, and no evidence of improvement over recent years despite increased training.[132-134] The Confidential Enquiry into Maternal and

Child Health (CEMACH) highlighted information on death certificates to be inaccurate or insufficient in around a third of cases reviewed.[44] There is also known to be variation in the quality of death certificate completion by cause, with self-harm shown to under-reported,[135] and deaths due to infections over-estimated, with a large proportion actually attributable to underlying medical conditions.[13,136,137]

Following concerns regarding the process, (primarily in relation to patient safety[138-141]), attempts to improve the quality and consistency of death certification have recently been undertaken throughout the UK. The Coroners and Justice Act 2009 set out plans to improve reliability and scrutiny of death certification in England and Wales with the introduction of Medical Examiners, which is being rolled out nationally from April 2019.[142] Medical Examiners are senior medical doctors who have undergone specific training in legal and clinical elements of death certification.[142] Their role is to ensure the content within the MCCD is accurate, notify the coroner if required, and detect and report clinical governance concerns.[143] They are required to review all deaths not already referred to the coroner in a local area by scrutinizing medical records, discussing the case with the attending medical practitioner completing the MCCD, clarifying with the bereaved family if they have any concerns, and reviewing the MCCD.[143] A similar system to scrutinize a sample of around 14% of death certificates not reported to the Procurator Fiscal was introduced in Scotland in 2015 with the establishment of the Death Certification Review Service, run by Healthcare Improvement Scotland. Similar reforms to the system in Northern Ireland include appointing medical examiner to the coroner's office were undertaken in 2009.[144,145]

The introduction of the Medical Examiner system may have a considerable impact on death certification and potentially affect future analyses of time trends in mortality by cause of death. Between 2008-2014, a review of 8,000 deaths where Medical Examiners have been introduced resulted in changes to the wording of the MCCD in 83% of cases.[146] Changes to the MCCD which result in a different underlying cause of death after review by a Medical Examiner are also likely. A pilot study conducted by the ONS of 5112 deaths in 2011 found disagreement in the underlying cause of death assigned by the attending doctor and that determined by a Medical Examiner in 12% of cases, with substantial variation by cause.[147]

Updates and changes to the software used by ONS for coding of cause of death can also result in differences in mortality estimates. Since 1993, ONS have used automated systems to code cause of death in around 80% of cases outside the neonatal period, with the remainder coded manually. Between 2001-2014, ONS used Mortality Medical Data System (MMDS) ICD-10 provided by the United States National Centre for Health Statistics (NCHS), with minimal changes noted when this was updated in 2010.[127] In 2014 this software was replaced with IRIS, a system supported by Eurostat. An analysis to assess the impact of the introduction of IRIS within of a sample of 38,717 deaths in 2014 found significant differences between the two coding systems in multiple ICD10 chapters, including causes specifically relevant to CYP such as congenital disorders (11.7% increase in deaths in IRIS compared with NCHS).[148] A similar analysis to assess how updates to the IRIS system would affect coding in 2017 found large differences in deaths due to infections within a sample of 42,413 deaths.[149] Importantly, as these analyses did not disaggregate differences in coding by age, the relative importance of these to CYP is unclear, and time series analyses of CYP mortality by cause need to be viewed in this context.

When a death cannot be registered

Under some circumstances, deaths cannot be registered by the attending medical practitioner. In England, Wales and Northern Ireland, these deaths are referred to a coroner for further investigation, and in Scotland they are reported to the Procurator Fiscal. In England and Wales deaths are referred where: the cause is unknown; the deceased was not seen within two weeks by the medical practitioner certifying the death, or after the death; where the death may have been caused by an accident, self-neglect or neglect of others or industrial disease; where the death occurred during an operation or whilst under anaesthetic; where the death may have been suicide; where the death occurred during or shortly after police custody; where no doctor was available to certify the death.[127] Although not all child deaths are referred to the coroner or Procurator Fiscal, local guidelines often mandate discussing the death, in order to identify concerns around safeguarding.[150]

After referral, in England and Wales the coroner can either: agree the death was due to natural causes and allow registration to take place; order a post-mortem to help determine

the cause of death if unknown, when there was no medical practitioner in attendance, or following a referral by the police; or order an inquest. In England and Wales, a death cannot be registered until the inquest has taken place. If an individual is charged with an offence relating to a death, the inquest is adjourned until the outcome of this is known, (although these deaths can be registered using temporary codes since 1977, a process called accelerated registration). Importantly, in Scotland these deaths can be registered as normal, with the cause of death later amended and referred to the Register for Corrections following an investigation.[127]

Interestingly, although there is a requirement for a coroner to hold an inquest when the death considered "unnatural" there is no agreed statuary definition for what this means.[151] This can result in inconsistencies between the threshold for undertaking inquests, (as highlighted in CEMACH[59]), and in turn contribute to variation in delay in registering deaths. Criteria and possible outcomes following referral of deaths to the coroner or Procurator Fiscal in Scotland and Northern Ireland are similar to England and Wales. However, there are large differences between the proportion of total deaths referred. In England and Wales, around 40% of all deaths are referred to the coroner[152] compared with around 29% in Northern Ireland,[153] and around 18% of deaths registered in Scotland reported to the procurator fiscal.[154]

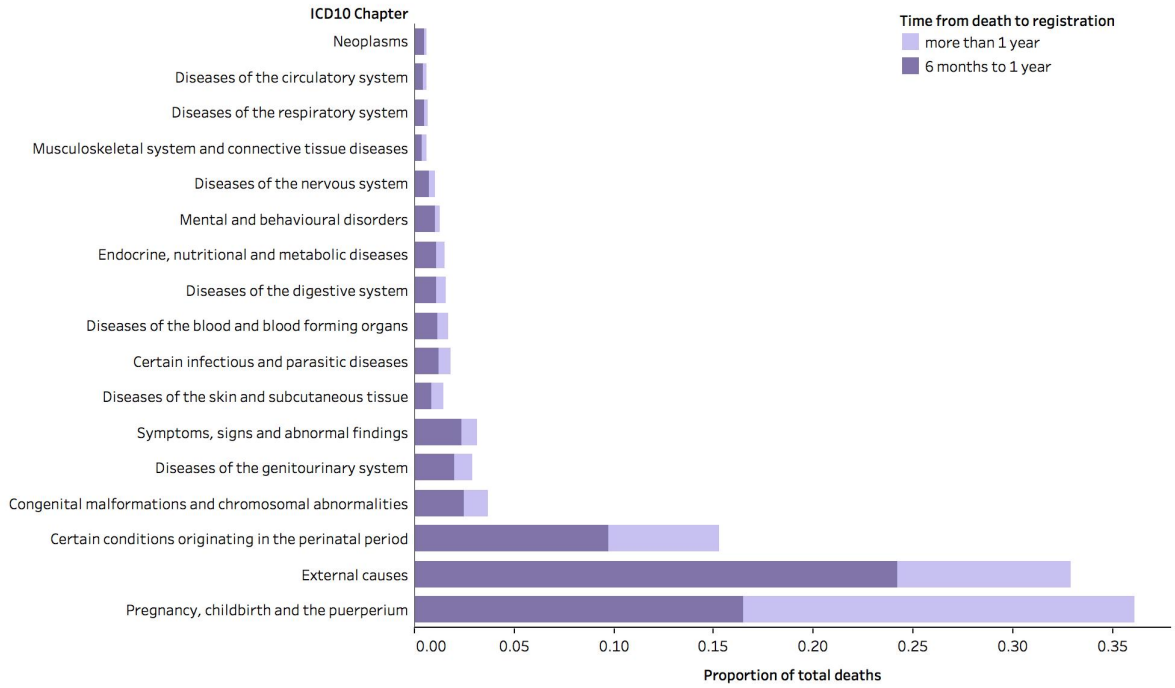
Following an inquest, coroners can also identify factors which they consider may prevent future similar deaths, and inform the individuals or authorities with the power to take interventions they feel are required. Prior to 2008 this practice was directed within Rule 43 of the Coroners Rules 1984 and undertaken at the discretion of the coroner.[155] However, the system has been expanded and strengthened in recent years, and so opportunities to learn from individual deaths has increased. The Coroners (Amendment) Rules 2008 placed a statutory duty on coroners to report concerns where identified, inform the Lord Chancellor of these, and required recipients of Rule 43 reports to respond within 56 days.[155] Rule 43 reports were then replaced with the introduction of Reports on Actions to Prevent Future Deaths (PFD) following The Coroners and Justice Act 2009 and Coroners (Investigations) Regulations 2013 (regulation 28). PFD reports further widened the remit and scope of this system, and increased the responsibilities placed on coroners to identify preventable factors and guide appropriate interventions when investigating a death.[156]

Delay in death registration

According to aggregate data provided by ONS, more than half of deaths in England and Wales are not registered within 5 days (as is legally required), with this proportion increasing over time.[128] Long delays are rare, with 99.7% of deaths registered within 1 year in 2018.[157] However, where deaths are referred to the coroner, particularly when an inquest takes place, the potential time lag between occurrence and registration can be considerable. Bird et al. previously estimated there to be at least a 6-month delay in registration of around 10,000 deaths per year in England and Wales, with this occurring in around 20% of all deaths in 5-44 year olds.[158] Mortality due to causes of death highly relevant to young people, such as injury or accidents, will be particularly affected. For example, Bird et al estimated that around half of deaths due to suicide registered in a particular year will not have occurred in that year.[158] Failing to account for potential delay in registration may lead to underestimates of mortality rates and hinder international comparisons.[53]

To describe this in greater detail, I used individual death registration data provided by ONS,[159] and calculated registration delay as the number of days from date of occurrence to date of registration. Figure 2 (p.57) shows the proportion of all deaths between 2001 and 2015 in England and Wales where time from death occurrence to registration was greater than 6 months or 1 year, by ICD 10 chapter. Deaths around the perinatal period show the longest delays, but constitute a low proportion of total deaths in CYP (see figure 9-11, p.82-84). However, almost a quarter of deaths due to external causes, (which includes accidental injuries, non-accidental injuries and self-harm, and contribute to more 50% of all deaths in 10-24 year olds in the UK) were registered more than 6 months after occurrence; 9% of these deaths were delayed in registration by more than a year.

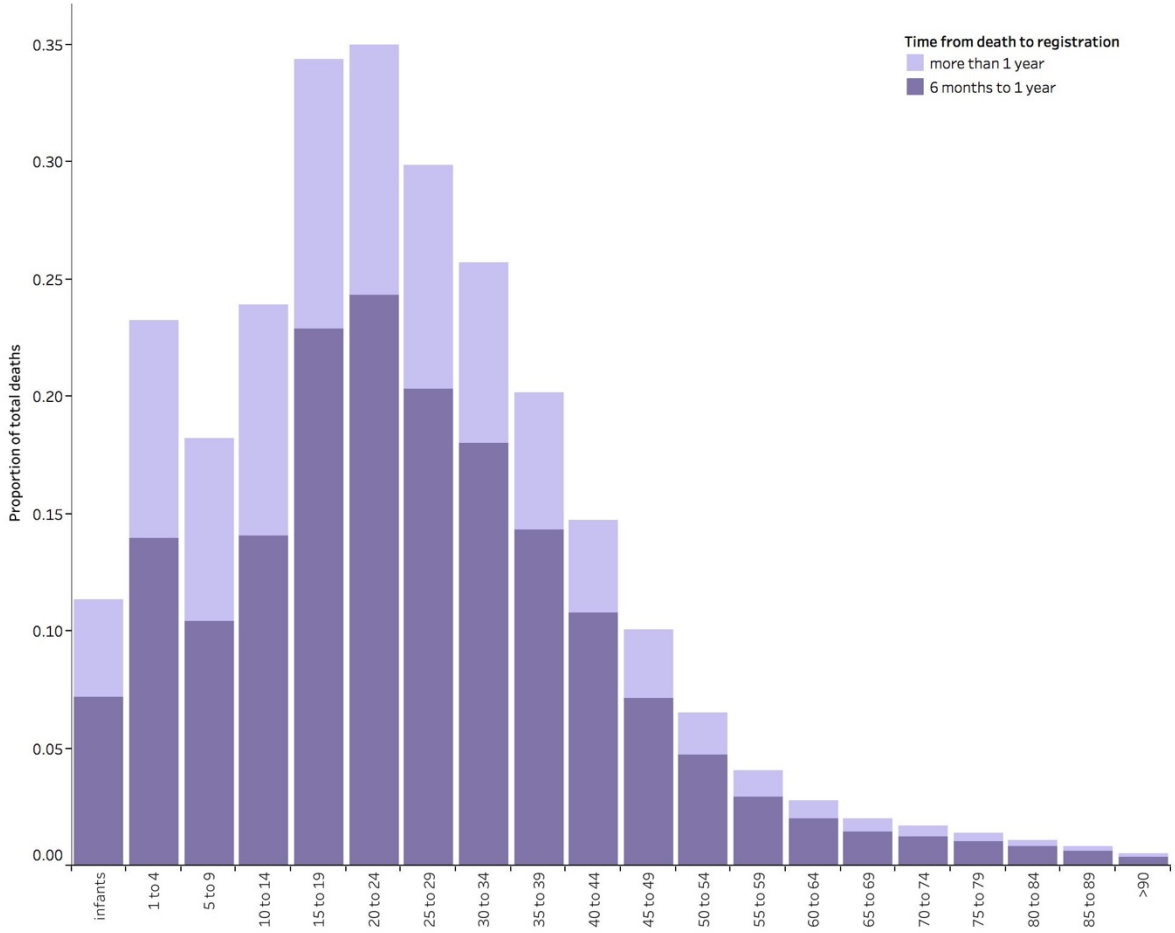
Figure 2: Proportion of all deaths in England and Wales between 2001-2015 where registration occurs more than 6 months after death occurrence by ICD 10 chapter.



Office for National Statistics. (2019). Death Registrations in England and Wales, 1993 – 2018: Secure Access. [data collection] 5th Edition. UK Data Service. SN:8200, http://doi.org/10.5255/UKDA-SN-8200-5

The changing predominant causes of death in children, adolescents and adults are then reflected in differences in registration delay by age group. Figure 3 (p.58) shows the proportion of deaths from all causes where registration took place more than 6 months after death occurrence by age group in England and Wales between 2011- 2015. Although this includes less than 5% of deaths in all those aged over 55, amongst 15-24 year olds more than a third of deaths were registered more than 6 months after occurrence, with around 10% taking more than 1 year till registration.

Figure 3: Proportion of all deaths in England and Wales between 2001-2015 where registration occurs more than 6 months after death occurrence by age group.

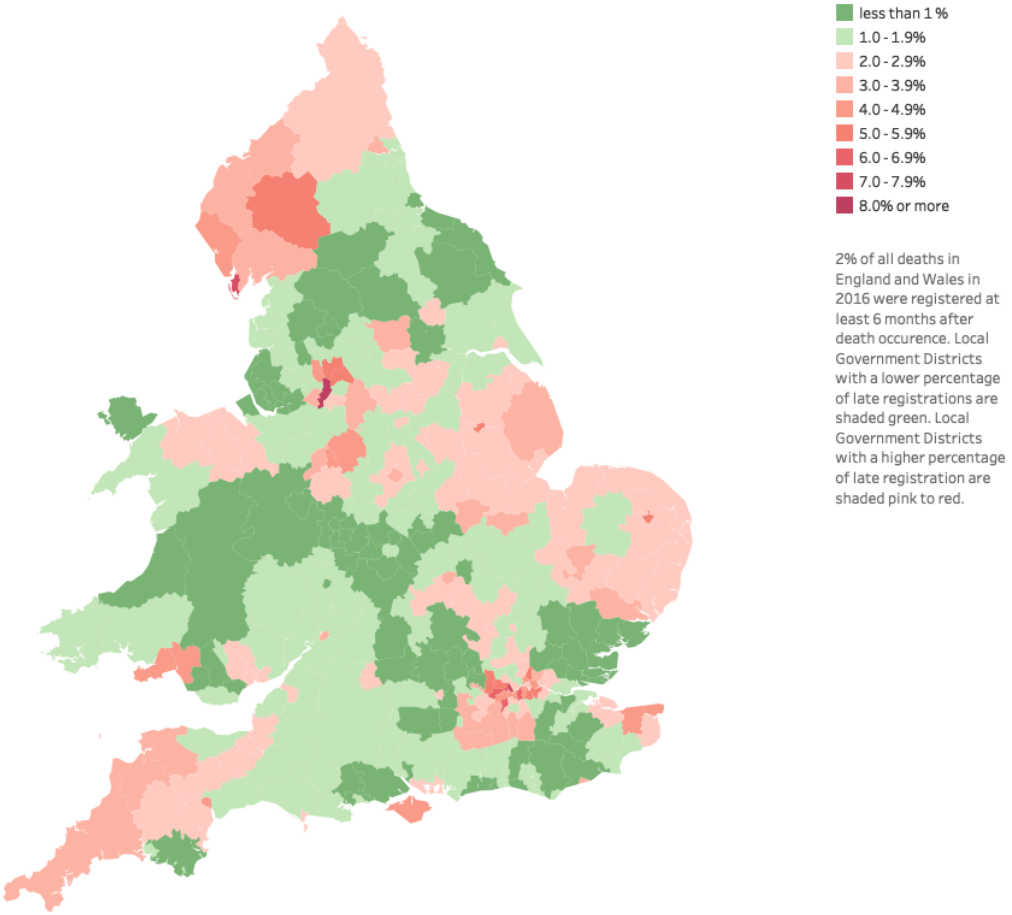


Office for National Statistics. (2019). Death Registrations in England and Wales, 1993 – 2018: Secure Access. [data collection] 5th Edition. UK Data Service. SN:8200, http://doi.org/10.5255/UKDA-SN-8200-5

Differences between the registration systems in Scotland, Northern Ireland and England and Wales can also have a large impact in registration delay. Using data to 2010, Hardelid et al. estimated 92.8% of post neonatal deaths were registered within 1 year of occurrence in England and Wales, compared with 99.9% in Scotland and only 70.5% in Northern Ireland.[53] The lack of appreciable delays in Scotland is likely due to the fact that unexpected deaths can be registered prior to the cause of death being established, unlike the rest of the UK (as described above).[128] Differences between the UK countries are even greater when specific causes of death are considered. For injury mortality amongst 15-19 males, the authors estimated 83.6% of deaths were registered within 1 year in England and Wales, compared with only 43.8% in Northern Ireland.[53] There is also considerable variation within the

countries of the UK, which may reflect differences in the quality of registration processes, but also demographic differences. Although in 2016 around 2% of all deaths in England and Wales were registered at least 6 months after they occurred, this ranged from 0% in Uttlesford, Essex, to 8.5% in Manchester (figure 4).[128]

Figure 4: Percentage of registrations in England and Wales occurring at least 6 months after death in 2016 by Local Government District[128]



Death registration systems in the UK compared internationally

Despite shortcomings described above, death registration systems used within the UK perform well when compared internationally. Phillips et al. devised the Vital Statistics Performance Index (VSPI) to compare registration systems between countries based on six domains: completeness of death reporting, quality of death reporting, level of cause-specific detail, internal consistency, quality of age and sex reporting, and data availability or

timeliness.[160] Using this metric, Mikkelsen et al. compared data reliability for death registration systems across 148 countries using data provided by the Global Burden of Disease study.[161] The UK system data quality and reliability was classified as "very high" in this analysis, ranking 10th overall for reporting in 2012. Although registration systems in most other high income countries also performed well, there is considerable variation which has implications for analyses described in this thesis. The VSPI rank for countries included in the comparator group for UK CYP mortality in Chapters 3 and 4 (the EU15+) ranged from Finland (2nd) to Greece (65th), with other countries performing poorly including Italy (64th) and Portugal (62nd).

Death registration in the UK: conclusions

The UK is fortunate to have well-established death registration systems with national coverage required by law. However, there remain large differences in the reliability and accuracy of these data. Cause of death registration coding continues to be highly problematic, and differences in the timeliness of registration vary between and within UK countries, by cause of death, and age group. These factors are particularly pertinent for adolescents, where the high proportion of injury and suicide mortality bias results of recently recorded deaths. The processes in the UK are also changing, and reform is likely to impact future analyses of trends in CYP mortality. In assessing current UK CYP mortality burden, variation in patterns of deaths within the UK, and international comparisons in outcomes, it is vital to consider limitations to death registration systems described here.

Death registration datasets used in this thesis

1. World Health Organization World Mortality Database. (WHO WMD)

WHO WMD are death registration data reported to the WHO by member states, and contain estimates for number of deaths by year, sex, age group, and cause coded to different iterations of ICD. Data are available for download, with population estimates also provided here: http://www.who.int/healthinfo/mortality_data/en/.

The main strengths of these data are that they provide a single repository for annual mortality estimates for most countries of the world, with good coverage for most high income countries

and data sourced from national death registration systems. Data estimates are also available from 1950, however completeness and latest data year is highly variable between countries. Data accuracy are subject to limitations within country death registration systems, as described above. I primarily use these data to describe current and long-term trends in UK all-cause CYP mortality, and current cause specific estimates, compared with other high income countries (Chapters 3 and 4).

2. Office for National Statistics

a) Office for National Statistics. (2019). Death Registrations in England and Wales, 1993 – 2018: Secure Access. [data collection] 5th Edition. UK Data Service. SN:8200, http://doi.org/10.5255/UKDA-SN-8200-5

This dataset provides details of death certification for all deaths registered in England and Wales from 1993 for all ages. Relevant data fields include demographic details, underlying cause of death, National Statistics Socioeconomic Classification (NS-SEC) for the deceased, (or parent), and location of usual place of residence and death (full post code). As with WHO mortality data, these individual level data are subject to limitations within the death registration process described above. These data were restricted, and required access to the UK Data Service Secure Lab.

There are multiple advantages to using individual level data provided within this dataset to population level estimates within the WHO WMD. Firstly, these data enabled delay in death registration to be examined by age group and cause of death, which is not available through other sources. Further, these data also allow socioeconomic differences in CYP mortality to be analysed at the individual level, and then contrasted with population level deprivation using the Index of Multiple Deprivation (IMD), which were provided separately by ONS (Chapter 6).

I applied to the UK Data Service secure lab for access to this dataset on 21st Feb 2018. My application was approved on 9th May 2018, I completed the UKDS Safe User of Research data Environments (SURE) ONS accreditation course on 2th May 2018, and received access to the

data on 1st June 2018. As per the terms of the data sharing agreement, these data can only be accessed and analysed within the UK Data Service Secure lab via https://sdslogin.essex.ac.uk, and from one IP address (194.82.246.67) situated within the UCL GOS Institute of Child Health, 1st floor office WTB, 30 Guilford Street, London WC1N 1EH. Request to output results are submitted through the UKDS, and must satisfy certain requirements including having a minimum of 10 units within each cell. Further details of access requirements can be found at https://www.ukdataservice.ac.uk. The data were updated on 18th September 2019 to include additional years of data.

b) Deaths by Index of Multiple Deprivation

I requested estimates for number of registered deaths in England from all causes by IMD quintile category and year of age (1-24) between 2001 – latest available (2018) from ONS. These are now publicly available, and downloaded on 23rd Jan 2020 from www.ons.gov.uk.

c) Office for National Statistics population data

Estimates for population for England by 5-year age group, sex, Index of Multiple Deprivation (IMD) category from 2001 – 2018 and by National Statistics-Socioeconomic Classification (NS-SEC) group 2002 - 2016 were requested from ONS, and are now publicly available on the ONS website (www.ons.gov.uk).

Local authority population estimates by ethnicity for 2016 were also downloaded from ONS (www.ons.gov.uk), and derived from the Annual Population Survey (2016) and UK census (2011).[162]

The Global Burden of Disease study

The Global Burden of Disease (GBD) study aims to measure health loss due to diseases, injuries, and risk factors, and describe these by sex and age within all countries of the world, and multiple subnational locations, over time. GBD was initially commissioned by the World Bank as part of the 1993 World Development Report: Investing in Health.[163] This represented the most comprehensive effort to quantify the world's health problems to date, and provided estimates for 1990 for 107 diseases in eight global regions and five age groups. Subsequent updates of the GBD, initially published by the WHO and then through the Institute of Health Metrics and Evaluation (IHME), have significantly broadened the scope of the enterprise. The most recent GBD update includes publicly available estimates for mortality, disability adjusted life years (DALY) and multiple other health metrics for 369 diseases and injuries in 990 locations, for 22 age groups and both sexes from 1990 to 2019, with further data available by request through the GBD collaborator network.[120] Outputs from GBD 2019 were developed using primary data from 86,249 sources including civil registration systems, vital statistics, censuses, disease notifications systems and household surveys, and then modelled to provide data points for location, years, age groups or causes of mortality or morbidity where primary sources are lacking. This work is produced in collaboration with a global network of over 5,500 researchers, providing country specific, disease or age group specific inputs to improve the estimation process. The methodology used to model these data in GBD 2019 is similar to GBD 2017 and GBD 2016, and described in detail within the main GBD capstone papers and supplementary material.[120] This includes procedures to standardise primary sources, redistribute non-specific or implausible causes of death, adjust for large spikes in mortality due to conflicts or natural disaster, and model estimates for locations lacking primary data. Details of all GBD 2019 locations, metrics and measures, and the individual data sources included in the estimation process, are available at www.healthdata.org. The GBD 2019 complies with the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) statement.[164]

Global Burden of Disease Datasets used in this thesis

Where possible I use observed death registration data to describe CYP mortality in this thesis provided by the ONS or WHO WMD. When this is not possible however, I use these modelled

data provided by the Global Burden of Disease. The key advantages for using GBD data are: 1) differences between ICD coding are reconciled in a standardized way to provide cause of death estimates spanning nearly 50 years; 2) they provide granular estimates for mortality within UK countries and English local authorities which due to the low numbers of death are not possible using ONS data described above; 3) they provide forecast estimates for mortality to 2040; 4) they provide modelled data for countries lacking primary mortality estimates.
GBD data are provided by the Institute for Health Metrics and Evaluation (IHME). Most are freely available for download from www.healthdata.org, however in addition I received estimates on request through the GBD Collaborator Network. Global Burden of Disease study 2019 (GBD 2019) provides estimates for number of deaths and mortality rate per 100 000 population with uncertainty intervals (UI) by sex and age group in 204 countries and territories (with data for 195 countries provided in GBD 2017). Subnational estimates are also available for many countries including the UK, where data are provided by UK country, English region and within 150 English Local Authorities. Mortality estimates for all-causes are available from 1950-2019, by cause of death from 1980-2019. Within GBD 2016, forecasted mortality estimates are also available from 2016 – 2040.

I use GBD estimates in Chapter 3 to describe cause specific trends in UK mortality due to limitations within the WHO WMD in using different ICD versions across years. In Chapter 4 I use GBD data to describe forecast mortality in the UK compared with other high income countries from 2016- 2040, and in Chapter 5 and 6 to describe subnational variation in CYP within the UK. In Chapter 9 I then use GBD data to describe global mortality outcomes in young people (10-24) from 1950 -2019.

Hospital Episode Statistics (HES)

Hospital episode statistics (HES) are national administrative data of secondary healthcare use within England. The impetus to create a national centralized system to deposit data on hospital activity stems from the 1979 Royal Commission on NHS information services,[165] and the basis for the current data collection system was set up in 1982.[166] Initially only a 10% sample of hospital activity data were collected for planning and management services, with national coverage for inpatient activity only achieved from 1990. Following the introduction within England of the pay-for performance system *Payment by Results* in 2004, HES data have been primarily collected in order to reimburse healthcare providers for delivering services.

HES data are maintained by NHS digital who provide provisional outputs monthly and a final extract at the end of each financial year.[167] Datasets are available for inpatient activity (Admitted Patient Care), outpatient activity, Accident and Emergency (A&E), and adult critical care. NHS digital are able to link records across these datasets to the Register of Deaths in England and Wales, held by the Office for National Statistics (ONS), to analyse mortality outcomes for patients with a HES record. These mortality data will not include individuals who have not had a secondary care hospital attendance (and so a HES record) within the time the data extract is requested.

Admitted Patient Care

HES Admitted Patient Care (APC) contains data on all admissions requiring a bed to NHS hospitals in England, and independent providers (charitable and private sector providers) paid for by the NHS.[167] This does not necessarily indicate an overnight stay: around half of admissions involving CYP are discharged on the same day (so called “zero day” admissions).[168] The APC dataset covers over 98% of hospital activity in England from around 700 providers, and includes maternity data covering over 97% of all births.[165]

Data are derived from discharge summaries completed following the end of an episode of care under one consultant from the health care provider. Clinical data available include dates of admission and discharge, the method of admission (emergency, elective, transfer,

maternal), location of discharge, operation codes used to identify surgical procedures, and the primary reason for the admission. The primary reason for admission is defined as: i) the main condition treated or investigated during the relevant episode of healthcare and ii) where there is no definitive diagnosis, the main symptom, abnormal finding or problem.[169] These are coded using ICD by coders who have undergone accredited training and follow standardized rules for translating discharge summaries to clinical codes.[167] In addition to the primary diagnosis, patients can be coded with up to 20 co-morbidities.[167] As hospital providers receive additional reimbursement for admissions with complex medical histories, there is a financial incentive to increase the number of diagnostic codes for admitted patients. In addition, the treatment (TRETSEF) and main specialty (MAINSPEF) of the admitting consultant is provided, allowing care episodes to be defined by medical specialty.

Admitted Patient Care data structure

Each row within the APC dataset refers to part of a hospital admission requiring a bed under one consultant. When a patient is discharged from the care of that consultant, this is referred to as a finished consultant episode (FCE). An *Inpatient Provider Spell* refers to FCEs within the same healthcare provider (i.e. an NHS trust), which may include multiple hospital sites.[167] The majority of CYP within HES are admitted and discharged under the same consultant within the same provider. However, patients can be transferred to the care of a different consultant, or have multiple consultants simultaneously, during a hospital stay. An *Inpatient Provider Spell* ends when a patient is discharged, transferred to another provider, or dies. Continuous inpatient stays are determined by first linking consecutive FCEs within each Inpatient Provider Spell, and then linking each consecutive *Inpatient Provider Spell* (from different NHS trusts), prior to discharge or death.

Outpatient Data

The HES outpatient dataset includes all NHS outpatient activity in England, and English NHS commissioned outpatient activity in the private sector.[165] This includes treatment funded by the NHS but carried out elsewhere, and private activity within NHS trusts.[170] Each observation indicates a planned appointment, and so includes all appointments which were either attended, cancelled, or not attended. Clinical data include the specialty of the consultant

providing the care, the primary diagnoses, the outcome of the consultation (discharge / further follow up) and the source of the referral. Note that other diagnostic fields within this dataset are poorly completed.[165]

Accident and Emergency

HES Accident and Emergency (A&E) datasets include all attendances to Major A&E Departments, specialty A&E departments, walk in centres and minor injury units.[165] Attendances are defined as planned or unplanned, and the outcome (admitted, transferred, discharged, left before being seen) is also provided. Although some data on diagnosis and treatments received within a department are available, these are poorly completed.

Demographic variables

In addition to clinical details described above, data are provided within each HES dataset on demographic variables including age (in years) at the time of healthcare use, ethnicity (although these data are often missing), usual place of residence (by Lower Super Output Area) and Index of Multiple Deprivation (IMD).

HES Data Cleaning Procedures

HES data are cleaned in the following steps:[171] Firstly old or invalid provider organisations are merged or amended. Duplicate records are then removed, although these are only those that have been sent multiple times to NHS Digital, rather than records duplicated at the point of collection. Records where there are duplicates in terms of cleaned provider code (PROCODE), AND either NHS number, local Patient Identifier, or postcode and date of birth and sex are identified AND NHS organisation Code (CDS: Commissioning Data Set Identify). Records must also be repeated within the following fields to be classified as duplicates: arrival data and arrival time (Accident and Emergency); episode start date and episode end date (Admitted Patient Care); appointment date, appointment time, main specialty, treatment specialty, consultant code, first attendance flag and whether the patient attended or did not attend (Outpatients). Where duplicates are identified, the latest submission is assumed to be the most reliable, and earlier records are removed.[172]

Common data quality errors are then identified and amended (Correction and Validation), according to data cleaning rules for each field which are published by NHS digital.[173] Finally, variables such as geographic data items are derived from the data extract from providers (Derivation) and HES patient Identification numbers are assigned using multiple different patient identifier fields. The pseudonymised HES ID is then derived from the NHS number and other identifiers. [165]

The HES data quality team then conducts a feedback and approval process with providers who have submitted data. For example, where there are suspected duplicate records, providers are given the opportunity to refuse the removal of these records in the final data release.[172] NHS digital has published annual guidance reports on known issues within the HES datasets since 2012 in order to monitor quality and recommend changes to the data submission process to improve it.[165] The accuracy of data submitted to HES is the responsibility of the health care provider, but NHS Digital has a legal responsibility to assess this set out in the Health and Social Care Act 2012.[165]

Data quality and completeness

Since its inception, there have been major concerns regarding the quality, consistency and reliability of data held within HES Datasets.[174-176] There are known to be large differences in coding practices between providers, particularly for co-morbidities,[177,178] and ongoing concerns around a lack of clinical engagement with the coding process.[179,180]

Results from the national clinical coding audit programme in 2009 estimated primary diagnoses amongst admitted patients were incorrectly recorded in 12.7% of cases,[181] but with considerable variation across the 4 clinical domains included (Trauma and Orthopaedics, Gynaecology, Urinary Tract and Male Reproductive System and Large Intestinal disorders, range 3.3 – 20% incorrect).[181,182] Further, data inputs to HES data from discharge summaries is highly variable. One systematic review of discharge coding accuracy identified 32 studies where routinely collected diagnostic or procedural codes were compared with disease registry data or case note review. Overall median coding accuracy was estimated at 83.2%,

but with substantial range (Inter Quartile Range 63.3 – 94.1%) and variation between procedural or diagnostic codes.[183] Completeness of HES records is also inconsistent. One recent study found only 83.1% of 4922 outpatient appointments identified through a review of medical records for prostate cancer were also identified within HES, increasing to 87.5% in a subset of cases recorded after 2008 (when the dataset was accredited as having national coverage).[170] Within HES Outpatients, although source of referral and main specialty are completed in >95% of observations, main procedure is only completed in 26% of records, and primary diagnoses in only 5%.[165]

As there has been considerable improvements to the quality assurance processes within HES data, there is likely to be temporal variation in the reliability and accuracy of results.[165,184] There are also changes to reporting specifications and incentives to report different fields over time, which may introduce further differences over time.[165] Following the introduction of Payment by Results in 2004, errors in coding can significantly affect funding accuracy for acute NHS trusts,[165,176] and there is some evidence this this has improved coding accuracy for some fields.[53,183] There are also concerns that data quality may differ between HES datasets; the relatively new additions of HES Outpatients and HES Accident and Emergency (with national coverage only achieved from 2008 and 2012 respectively) may result in more coding error than the better established HES APC dataset.[170] Further, as there are greater cost incentives for accurate inpatient coding, these are likely to be of higher quality.

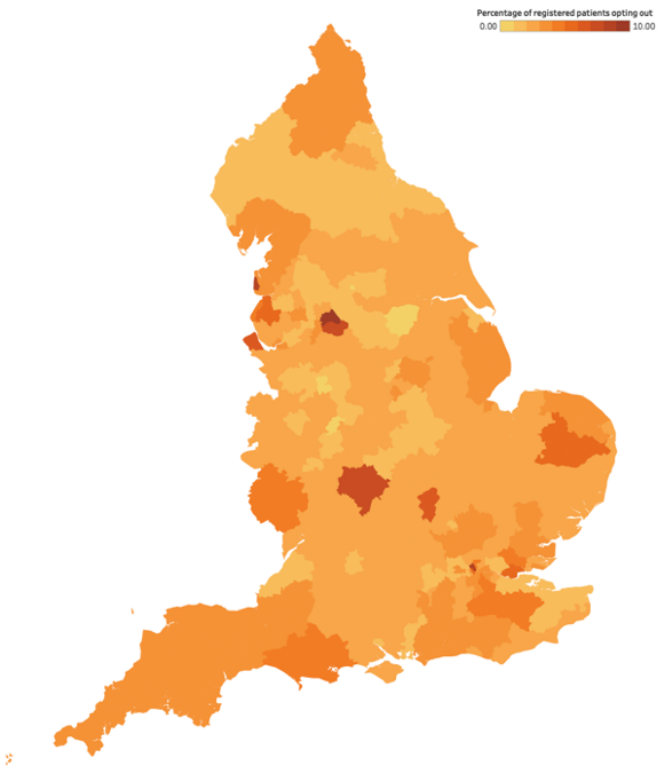
National Data Opt Out Programme and Type 2 Opt Outs

HES data are collected without consent primarily for the purposes of reimbursing trusts for providing health services. Although these contain details of almost all secondary care activity in England, there are limitations to the availability of these data for research purposes. Following recommendations from the National Data Guardian,[185] patients can request that confidential information held by NHS Digital is not shared for purposes other than clinical care. This system was formalised in Jan 2014, with the introduction of an opt out system. Patients were able to opt out through their GP for their data being shared outside their GP practice (type 1 opt out) or outside of national databases (i.e. NHS Digital). This was extended to include all organizations that use health and care information in May 2018, with the

introduction of the National Data Opt Out Programme, which allows patients to set their national opt out preferences via an online system.[186] When a patient opts out, all previous and subsequent observations within HES databases made available for analysis will be removed, and so the number of observations for a given year is partly dependent on the extraction date.

Opt outs have the potential to introduce selection bias to analyses using HES as they are not randomly distributed. Piel et al. analysed type 2 opt out prevalence within APC, outpatient and A&E HES datasets. Type 2 opt out prevalence increased in patients who were older (over 60), female sex, higher socioeconomic status, and whose ethnicity was recorded as black, compared with white or Asian.[186] There is also wide geographic variation in opt outs; in 2019, the prevalence of opt outs within NHS Clinical Commissioning Groups ranged from 0.3% in NHS Bradford City CCG, to 10.0% in NHS Oldham CCG (figure 5). The national rates of opting out have been increasing over time, although the explanations for this remain unclear.[186] In March 2019, (at the time the HES data were extracted for the purposes of this project), 1.63% of 0-9 year olds and 1.85% of 10-19 year olds were registered as opting out.[187]

Figure 5: Percentage of registered patients opting out by CCG in 2019



Hospital Episode Statistics datasets used in this thesis

I requested data for all secondary care contacts within Hospital Episode Statistics (HES) datasets for all children and young people aged 0-24, linked to death registration data. Due to the cost of the data, the years requested were limited to 2007/08 to 2018/19 for HES Admitted Patient Care, HES Outpatients, HES Accident and Emergency from and HES Critical Care from 2008/09 (the first year data were available) to 2018/19.

All HES data fields requested were pseudoanonymized: age at healthcare contact was provided in years (with date of birth not provided), and usual address was provided at the level of Lower Super Output Area (LSOA). Patient names were replaced with a unique encrypted HES-identity number provided by NHS digital, to allow the five datasets to be combined and follow individuals through different healthcare contacts over time.

Consent is not sought to use HES data for research purposes. However, as the data requested did not include identifiable variables, I received confirmation from NHS digital that Confidential Advisory Group (CAG) support under section 251 would not be required on Monday 13th August 2018

As a requirement of the NHS Digital application, and in order to comply with the General Data Protection Regulation (GPDR), a publicly available transparency statement describing the project aims, legal basis for the use of personal health data, and details of how to opt out of using NHS data for research purposes, has been uploaded to my UCL Institutional Research Information Service (IRIS) webpage here: https://iris.ucl.ac.uk/iris/browse/researchActivity/23320.

The NHS Digital Data Access Request Service application (ref DARS-NIC-141410) was submitted on Friday 24th August 2018. I was informed the application was successful on 14 Jan 2019. The invoice for the final cost for the data at £22,368 was received on 13th Feb 2019, and the data were downloaded and transferred to the UCL Data Safe Haven for analysis on 20th May 2019.

Details of the legal basis for using these data, and how the use of these analyses comply with the General Data Protection Regulation (GDPR) are provided in supplementary material 1.

I use these data to describe trends in healthcare use in CYP in England, and specifically within causes where the UK has high CYP mortality compared with other high income countries. The specific methods for these analyses are described in Chapter 7 and 8.

Public and patient involvement

I organised a Patient and Public Involvement and Engagement initiative for this project, and presented the research proposal, methods and planned use of data described above to members of the National Children's Bureau Young Research Advisors (YRA) group in March 2018. I did this to improve my understanding of issues relevant to young people with respect to using confidential data without consent, and to inform the application for HES data from NHS Digital and the Research Ethics Committee submission for this work.

The YRAs are a diverse group of CYP recruited from across the country who have received training in research methods and policy. Further information regarding the YRAs and their involvement in research projects are available via the NCB website (www.ncb.org.uk).

I held a focus group of 25 young people aged 7-22 and their parents to discuss the acceptability of the research methods. Following a presentation of the project, the YRA group were given the opportunity to ask questions and clarify the plan for the project. The CYP were then split up in to smaller groups to provide specific feedback regarding the use of data without consent (needed for the HES analysis), the information included in the presentation, and how best to inform young people of the results. The main points raised were as follows:

Information regarding the project

a) The majority of CYP involved felt the information included in the presentation and the aims and purpose of the research were clear and understandable. They did ask for clarity on certain points, which will inform future dissemination of the results to CYP.

Use of Data without consent

a) The CYP were well informed about data use for research, and the need to seek consent if this is possible
b) The CYP present acknowledged if it is not possible to seek consent, this should not prevent research from happening
c) The CYP felt it was important to keep the data anonymised when reporting
d) They trusted the systems in place to keep their data secure (i.e. within UCL)
e) CYP would like more generic information that their data may be used in this way (e.g. when they see their GP / visit hospital)

Informing CYP regarding the results

a) The CYP were keen to be included in further dissemination plans in collaboration with the National Children's Bureau (NCB) who have offered to support this. I plan to follow this up after completion of this thesis.

Summary

Completing this PPI initiative supported the NHS Digital and REC applications, and also gave me my first experience of including young people in the research process. The young people who attended this focus group were engaged with the aim of this project, and supported the use of their data for this purpose. They also provided useful ideas to develop future projects related to this work, and were keen to be included in dissemination of the results.

Research Ethics and Confidential Advisory Group Support

This study involves secondary analysis of routinely collected data. The main ethical, legal and management issues arising from this project relate to data security for sensitive data needed for some of the analyses.

The study was reviewed by the London-Brent NHS Research Ethics Committee (NHS REC) on 23rd Jun 2018, and received a favorable opinion on 3rd August 2018. I have received confirmation that review by the Health Research Authority is not required. The study has also been reviewed by the Confidential Advisory Group (CAG) in regard to the use of personal data

without consent, and approved for support under section 251. However, I had confirmation from NHS digital that this will not be required. Details of NHS REC, CAG, and HRA correspondence is shown in supplementary material 1.

Chapter 3

Deaths in children and young people in the UK

Exploring mortality differences between the UK and other countries requires an understanding of the how UK burden of deaths varies by age group and sex, and of trends over time. Here I will describe a snapshot of deaths in children and young people (CYP) in the UK, and how these have changed from 1950 – 2016.

Chapter 3 methods

Where possible, I used primary death registration data provided by the WHO World Mortality Database to analyse CYP mortality in the UK. However, due to complexities around grouping causes of deaths using different International Classification of Disease (ICD) systems over time, I used Global Burden of Disease (GBD) data to describe longer term trends in the leading causes of death within each age group.

WHO World Mortality Database Data

I used number of deaths and mortality rate per 100,000 provided by the WHO World Mortality Database (WMD) to describe the current UK burden by cause of death in children and young people 1- 24, and trends in all-cause mortality from 1950. Data were accessed on 19th December 2019 from http://www.who.int/healthinfo/mortality_data/en/). The most recent data year for the UK was 2016.

Deaths were grouped according the Global Burden of Disease (GBD) mortality hierarchy (available in the supplementary material), which provides more meaningful classification than using ICD10 chapter heading alone. The GBD classifies deaths across 4 levels. For example, acute lymphoblastic leukaemia (level 4) is classified within leukaemias (level 3), neoplasms (level 2) and non-communicable diseases (NCD) (level 1). For this summary of CYP mortality burden, I grouped deaths across level 2 causes, with some causes subdivided to level 3 cause

where there were significant numbers of deaths in a specific age group (e.g. asthma, epilepsy, congenital birth defects and type of infection, cancer and injury).

Due to shortcomings of death registration systems described in Chapter 2, around 25-30% of UK CYP deaths within the WMD have causes of death which are considered to be inappropriate or illogical. In the Global Burden of Disease study 1990, Murray et al used the term "garbage code" to describe such deaths.[188] Multiple strategies have been proposed for redistributing these garbage codes to other "target" causes to improve the reliability of analyses, but there is little agreement as to which to adopt. I used a minimally modified version of the GBD2017 methodology for redistributing these garbage codes to each cause group (levels 1-4). I first classified garbage codes (level 1-4) as described by the GBD, and then proportionately redistributed deaths within each level for all causes, avoiding the need for detailed target cause lists for specific codes as used in the GBD.[189]

Level 1 garbage codes were defined as deaths unable to be assigned level 1 GBD category. I redistributed these deaths proportionately within each country, year, sex. and age group *across all causes*. Level 2 garbage codes were defined as causes of death where level 1 GBD category could be determined, but not level 2 category (e.g. unspecified injuries). I assigned these deaths a level 1 GBD category. These deaths were then redistributed within each country year sex and age group and level 1 GBD category. For level 3 garbage codes, (deaths where a level 2 category could be determined, but level 3 was unknown) and level 4 (deaths where a level 3 category could be determined, but level 4 was unknown), I assigned each cause a level 1 and level 2 GBD category. These deaths were then proportionately redistributed within each country, year, sex, age group, level 1 and level 2 category.

Where there were no appropriately coded deaths within a level 2 category for a country, year, sex, age-group, I redistributed level 3 and 4 garbage codes within their level 1 category only. Where there were no appropriately coded deaths within a level 1 category for a country year sex age group, garbage codes were proportionately redistributed across all causes. Where there were no deaths in *any* cause group for a country, year, sex, age-group, we were unable to use proportional redistribution, and these deaths were excluded (n=9).

Global Burden of Disease study data

To analyse long term trends in UK CYP aged 1-24 mortality by cause, I used data from the Global Burden of Disease study 2017, supplied on request by the Institute for Health Metrics and Evaluation (IHME). Mortality rates per 100,000 for 1-4, 5-9, 10-14, 15-19, 20-24 by sex were available from 1980 – 2017 by cause of death.[190] Although these estimates are based on primarily death registration data, they are also standardized within the GBD estimation process, and so will differ slightly from those available from the Office for National Statistics (ONS) and WHO WMD.[191] Specific details of the GBD estimation process, methods used to standardise data sources, and descriptions of the statistical models used to populate data gaps, are provided elsewhere.[1,190]

I used a similar method for classifying cause of death as with the WHO WMD analysis. I describe causes of death at level 2 of the GBD cause of death hierarchy described above, but modified this to analyse some important causes in greater detail which require different public health responses. Firstly, I analysed *Self-harm* separately from other causes within the level 2 group *Self-Harm and interpersonal violence*, which we subsequently refer to as *Interpersonal violence and conflict*. I also disaggregated the level 2 group *Maternal and neonatal disorders* by its two level 3 causes (*Maternal disorders* and *Neonatal disorders*).

Chapter 3 results

UK child and young person mortality in 2016 (WMD Data)

In 2016 there were 3627 deaths in CYP aged 1-24 in the UK, amounting to 19.2 deaths per 100,000 population. 64.8% of deaths occurred in males, with this proportion increasing with age (52.3% in 1-4 compared with 70.3% in 20-24). The number of deaths and mortality rate per 100,000 by age group and sex are shown in figure 6-8 (p.79-81). 78.7% of deaths occurred during adolescence (10-24); 45.1% in 20-24, 24.7% in 15-19 and 8.9% in 10-14. After 1- 4, mortality rates increased by age group in both sexes, but with less variation amongst females. There was a 6.8 fold increase in mortality rates in 20-24 compared with 5-9 amongst males, with only a 3.9 fold increase amongst females.

Number of deaths by cause in 1-4, 5-9, 10-14, 15-19 and 20-24 are shown in figure 9-13 (p.82-86). The most common causes of death amongst 1-4 in the UK in 2016 were congenital birth defects (16.7%), cancers (16.3%), transport injuries and other accidents (15.5%) and infections (15.3%), of which over half were due to lower respiratory tract infections. Amongst 5-9, cancers were the most common cause, accounting for 26.8% of all deaths, with around half of these being either due to leukaemia and brain / central nervous system malignancies. Amongst 10-14, the leading causes of death were cancers (27.2%) and injuries (25.9%). Amongst 15-19, more than half (50.4%) of all deaths were due to injuries, with a quarter (25.8%) due to either self-harm or interpersonal violence. Other important causes in this age group included cancers, which accounted for 15.6% of all deaths. Amongst 20-24, the proportion of deaths due to injury rises to 62.7%, of which more than a third (34.7%) are due to self-harm or interpersonal violence.

Figure 6: Number of deaths in 1-24 by age group in the UK in 2016

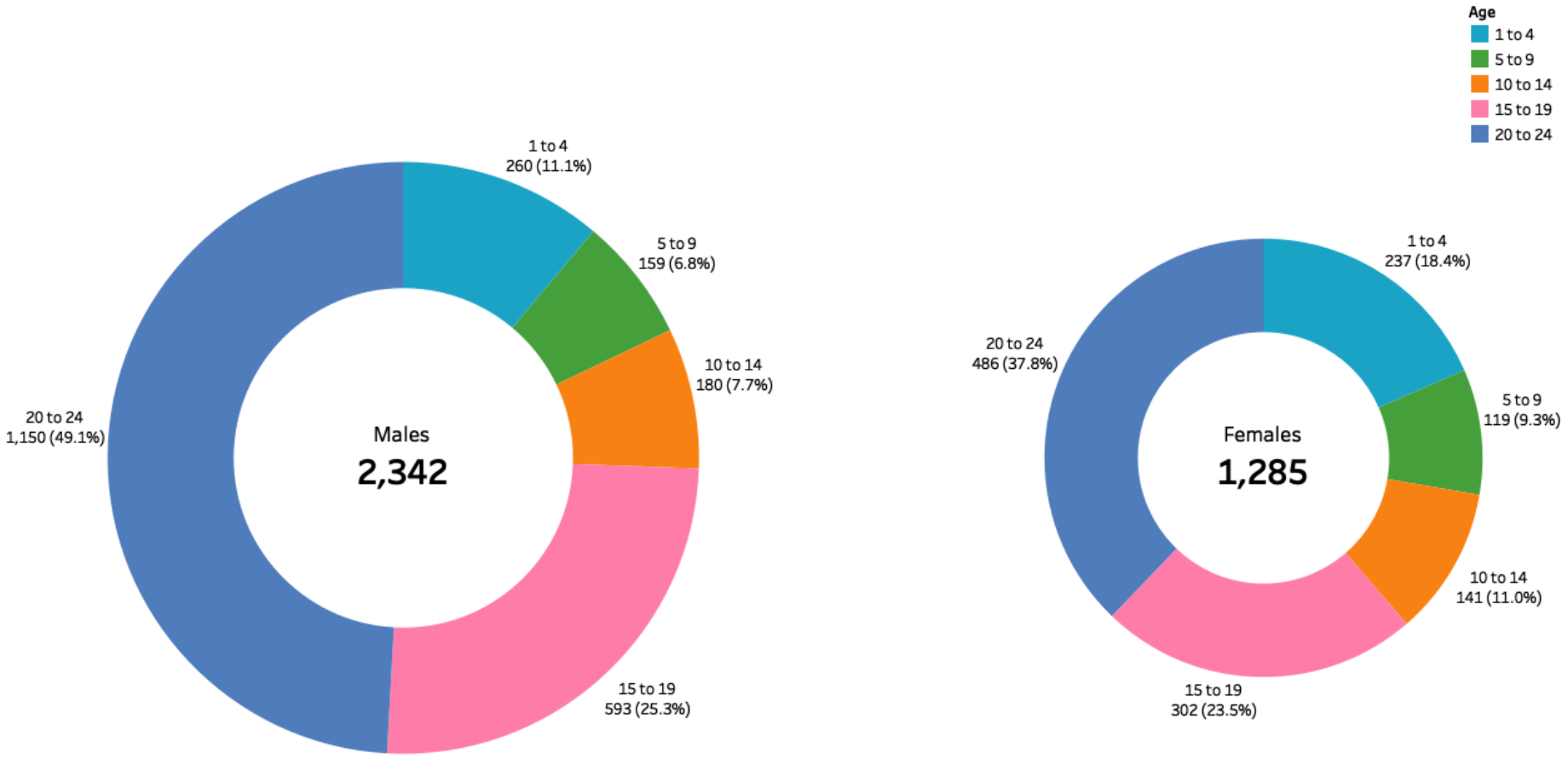


Figure 7: Distribution of deaths by sex in 1-24 year olds in the UK in 2016

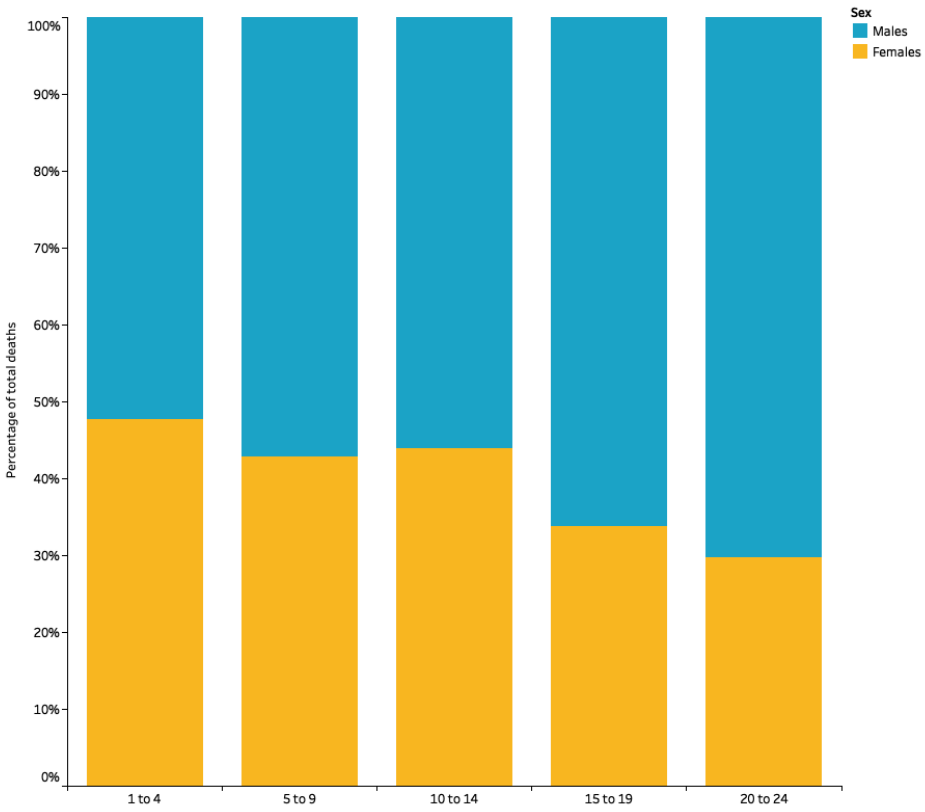


Figure 8: Mortality rate by age group and sex in 1-24 year olds in the UK in 2016

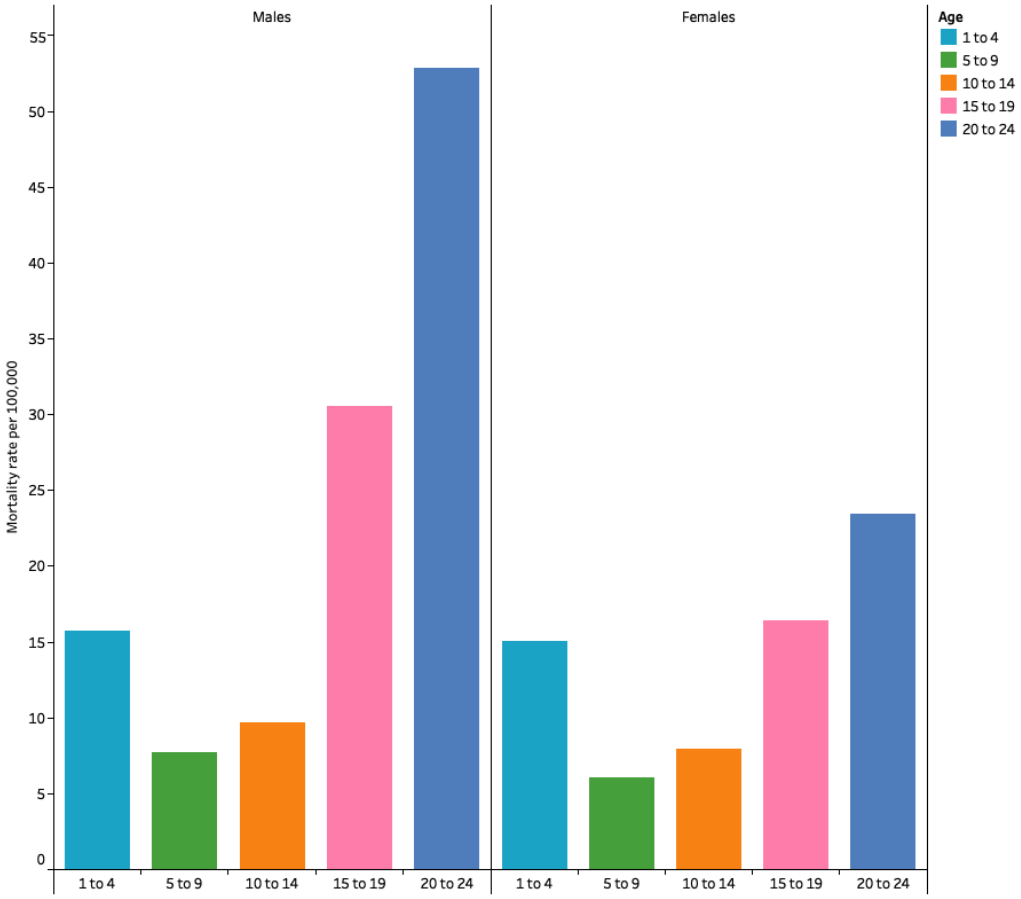


Figure 9: Number of deaths in 1-4 by cause in the UK in 2016 (both sexes)

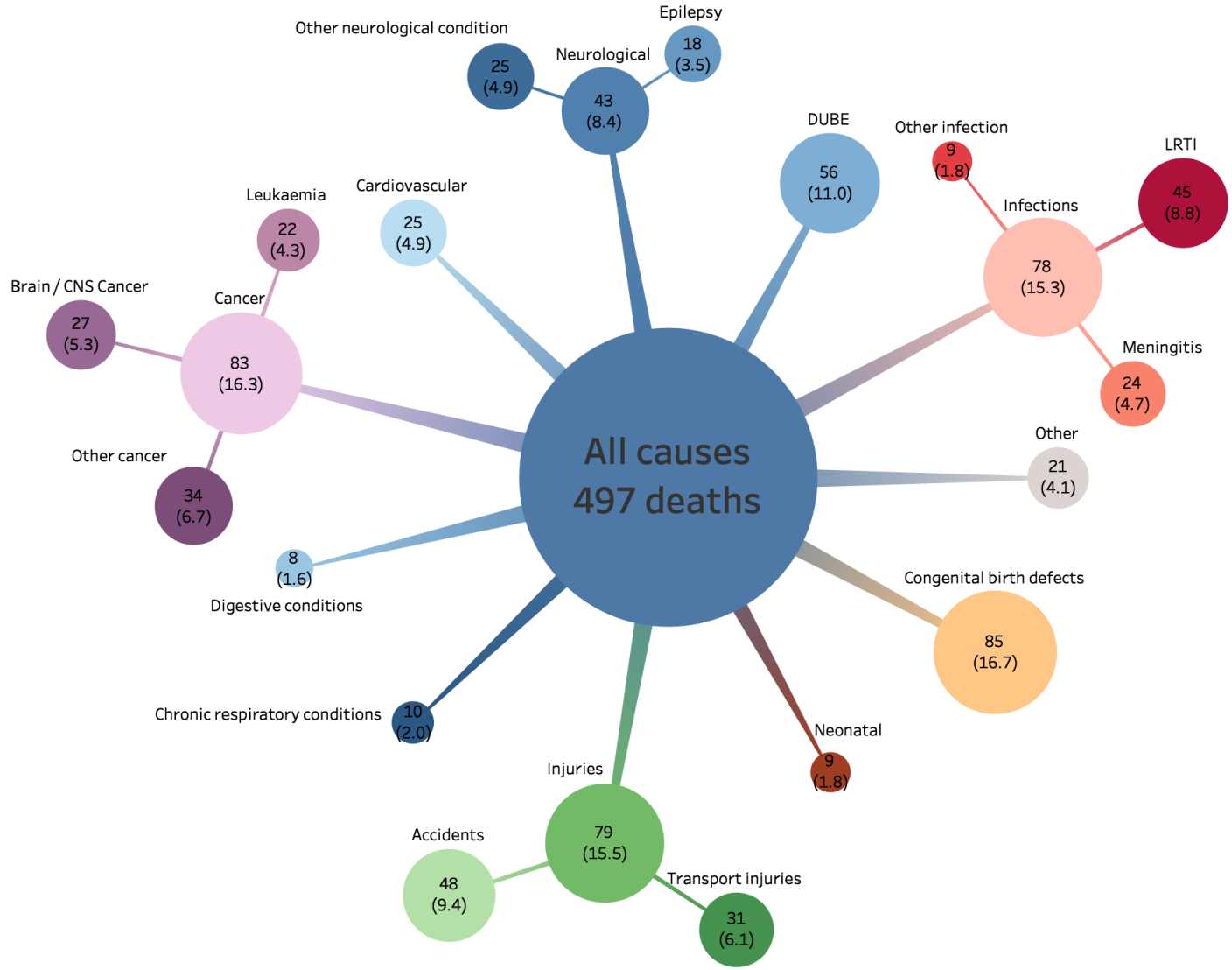


Figure 10: Number of deaths in 5-9 by cause in the UK in 2016 (both sexes)

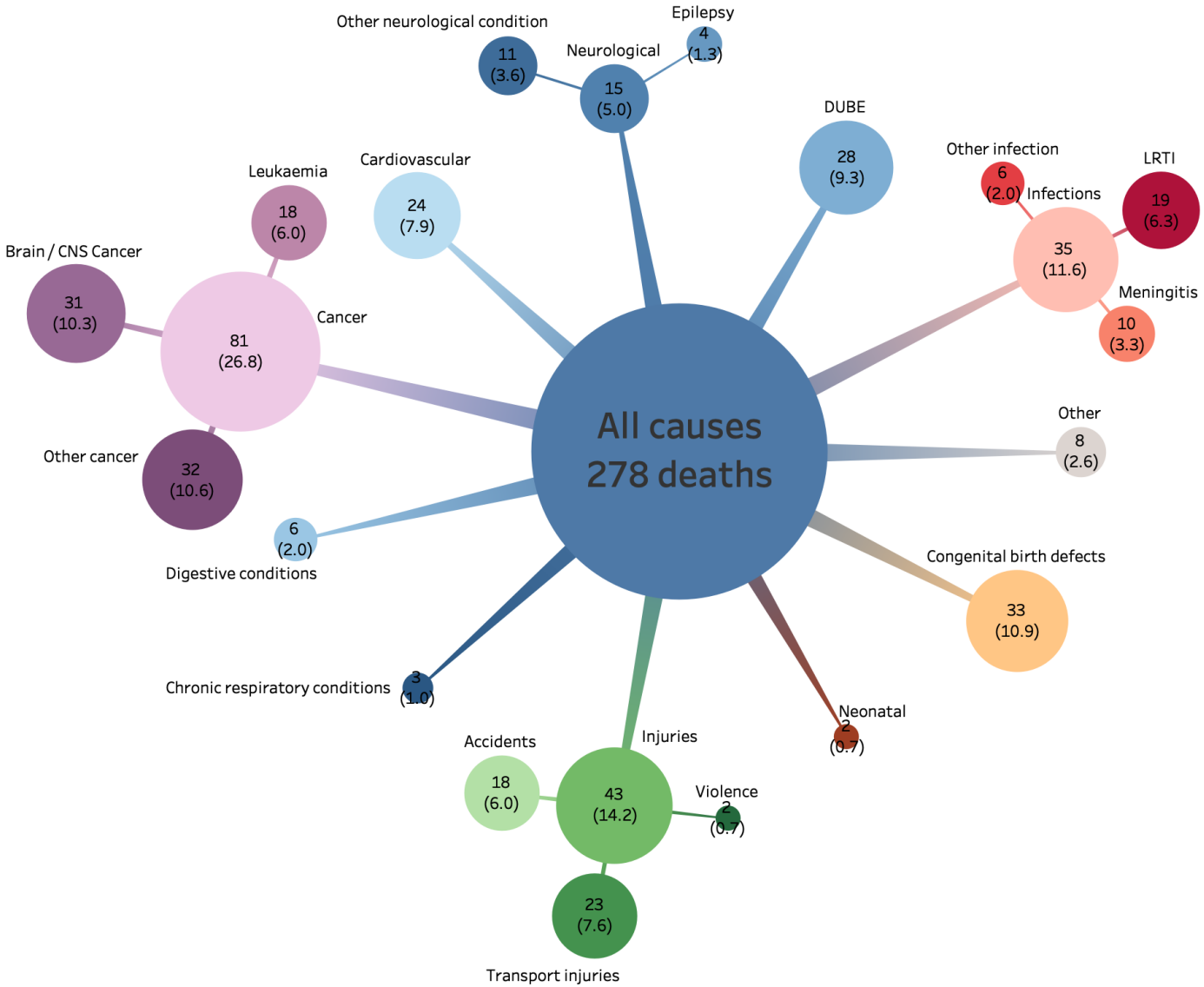


Figure 11: Number of deaths in 10-14 by cause in the UK in 2016 (both sexes)

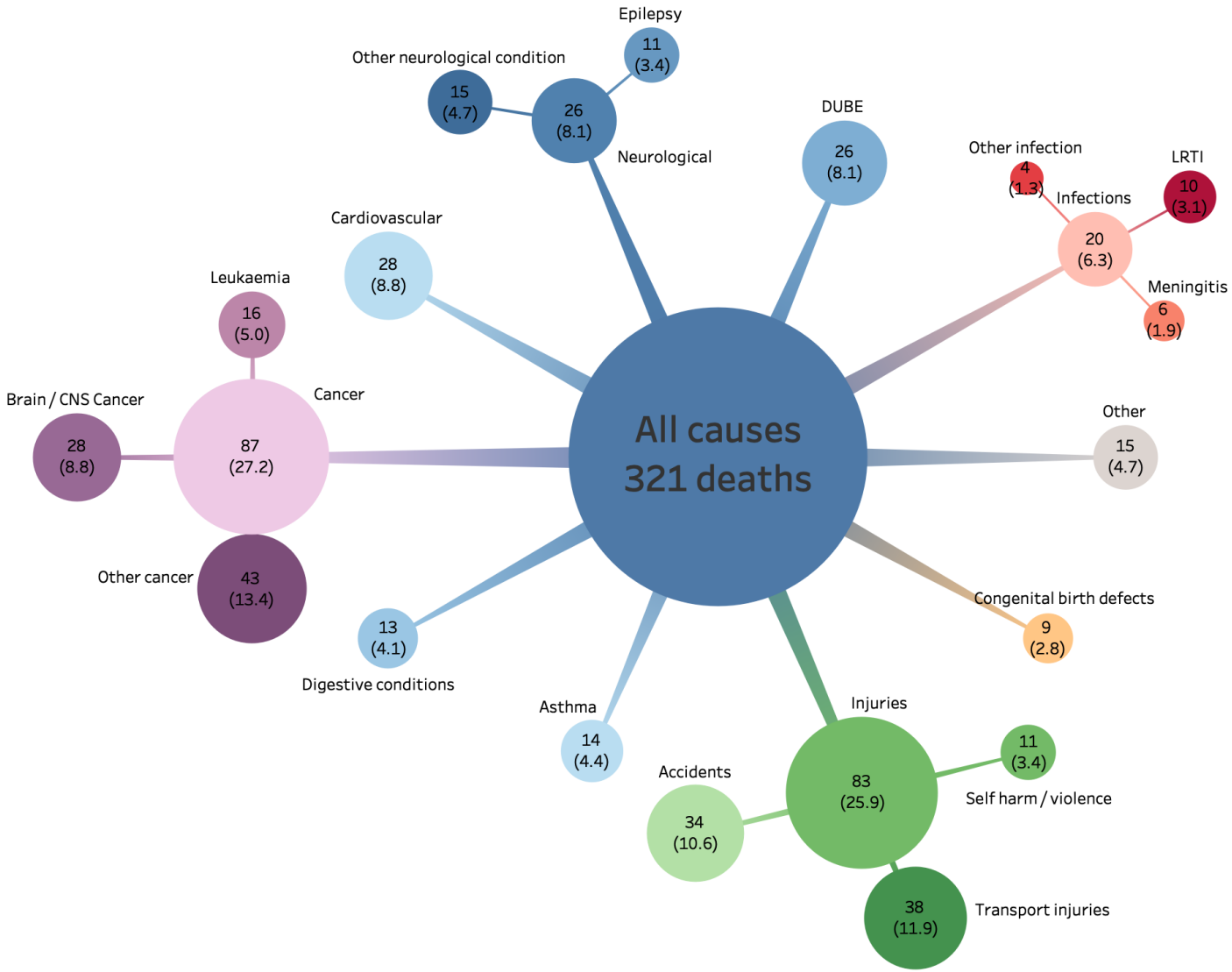


Figure 12: Number of deaths in 15-19 by cause in the UK in 2016 (both sexes)

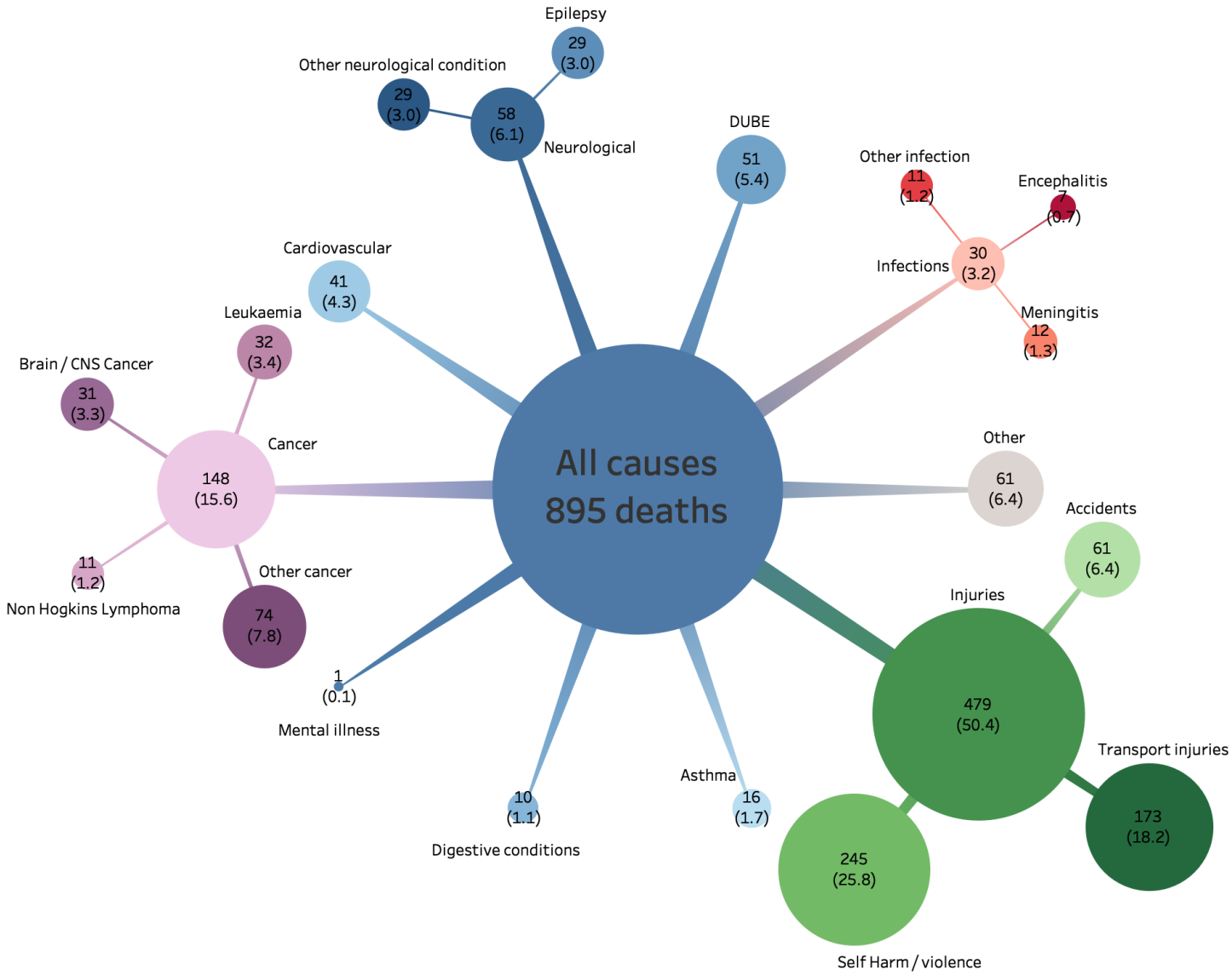
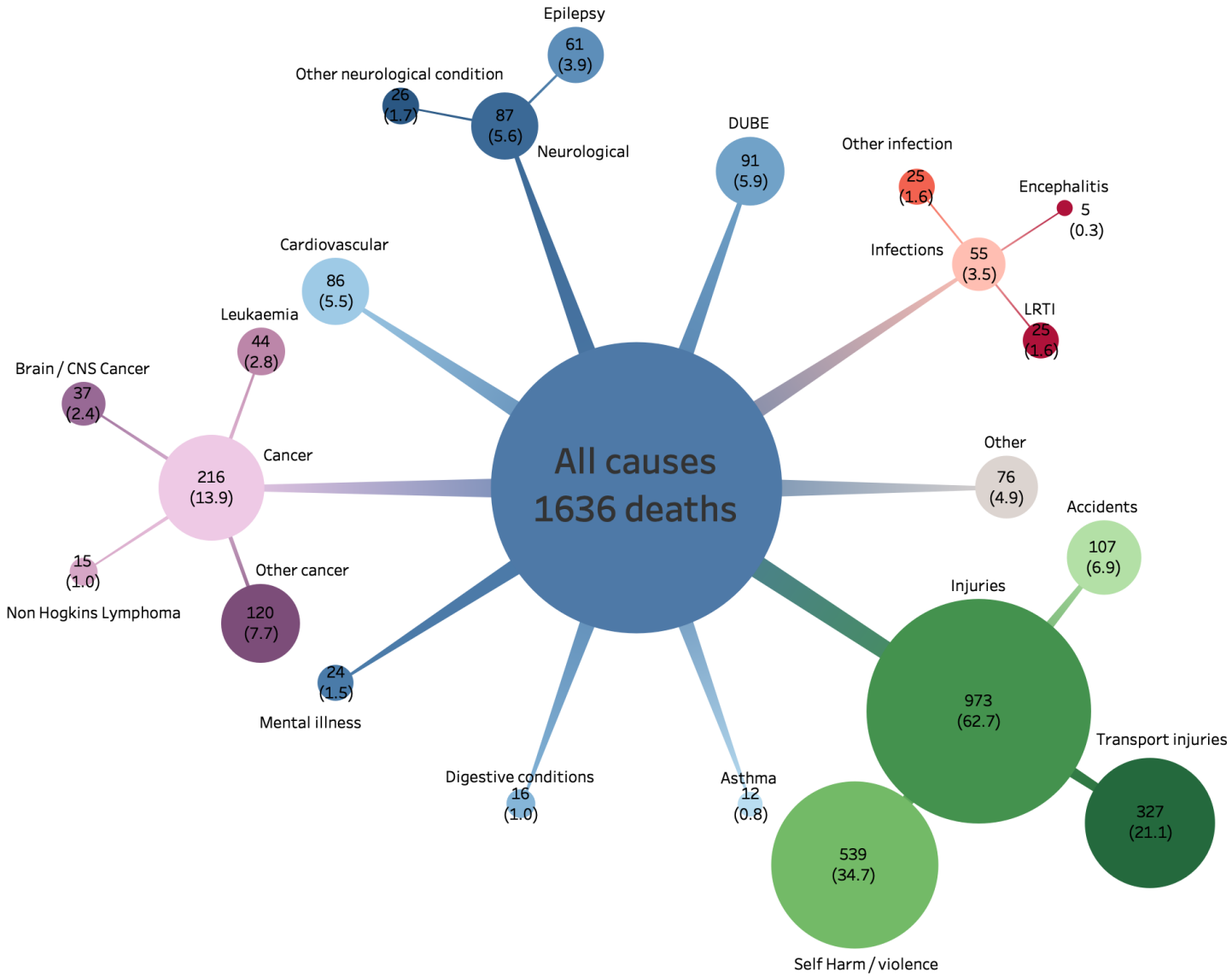


Figure 13: Number of deaths in 20-24 by cause in the UK in 2016 (both sexes)



UK child and young person mortality trends over time 1950 - 2016

Trends in UK child and young person mortality for all causes of death 1950 - 2016 (WHO data)

Mortality rate per 100,000 by age group and sex in the UK between 1950 and 2016 is shown in figure 14 (p.88). Mortality rates have declined sharply in all age groups, but with considerable variation by age group and sex. Amongst males, the mortality rate for 1-24 combined declined by 77.2% in males compared with 83.9% in females over this period. In both sexes, declines were greatest in younger age groups. In males, mortality rates declined by around 89% in 1-4 and 5-9 year olds, compared with declines of 82% in 10-14, 70.3% in 15-19 and 62.6% in 20-24 (the lowest decline in any age and sex group). In females, a similar pattern is shown with declines of around 88% in 1-4 and 5-9, compared with declines of between 80.4 – 80.7% in 10-24. As a result, mortality rates in 1-4 dropped below those of 20-24 and 15-19 from around 1970 amongst males, and 1990 in females, and mortality rates in 5-9 dropped to be similar to 10-14 from 1980 in males and females onwards. This is reflected in the proportion of CYP deaths occurring during adolescents, rising from 55.6% in 1950, to 78.6% in 2016 (figure 15, p.88).

Recent changes in mortality rate also appear to have affected adolescents differently to young children, within improvements stagnating over the last 5 years in this group. Figure 16 (p.89) shows annual percentage declines in mortality rate between 2011 and 2016 and 2001 and 2011 amongst males and females by age group. Between 2001 and 2011, all age groups experienced at least a 2% annual decline in mortality rate except 5-9 males, where the decline was 1.5%, and adolescents 10-24, who experienced between 2.2 and 4.5% annual reduction. Since 2011, these improvements appear to have dropped off in older age groups, in contrast to 1-9 year olds. The mortality rate in 20-24 has increased in three consecutive years since 2013 in males from 48.1 to 52.1, with a modest rise also seen in females 15-19 and 20-24 over this period from 15.7 – 16.4 and 20.9 to 23.4 respectively.

Figure 14: Mortality rate by age group and sex in 1-24 year olds in the UK in 1950 - 2016

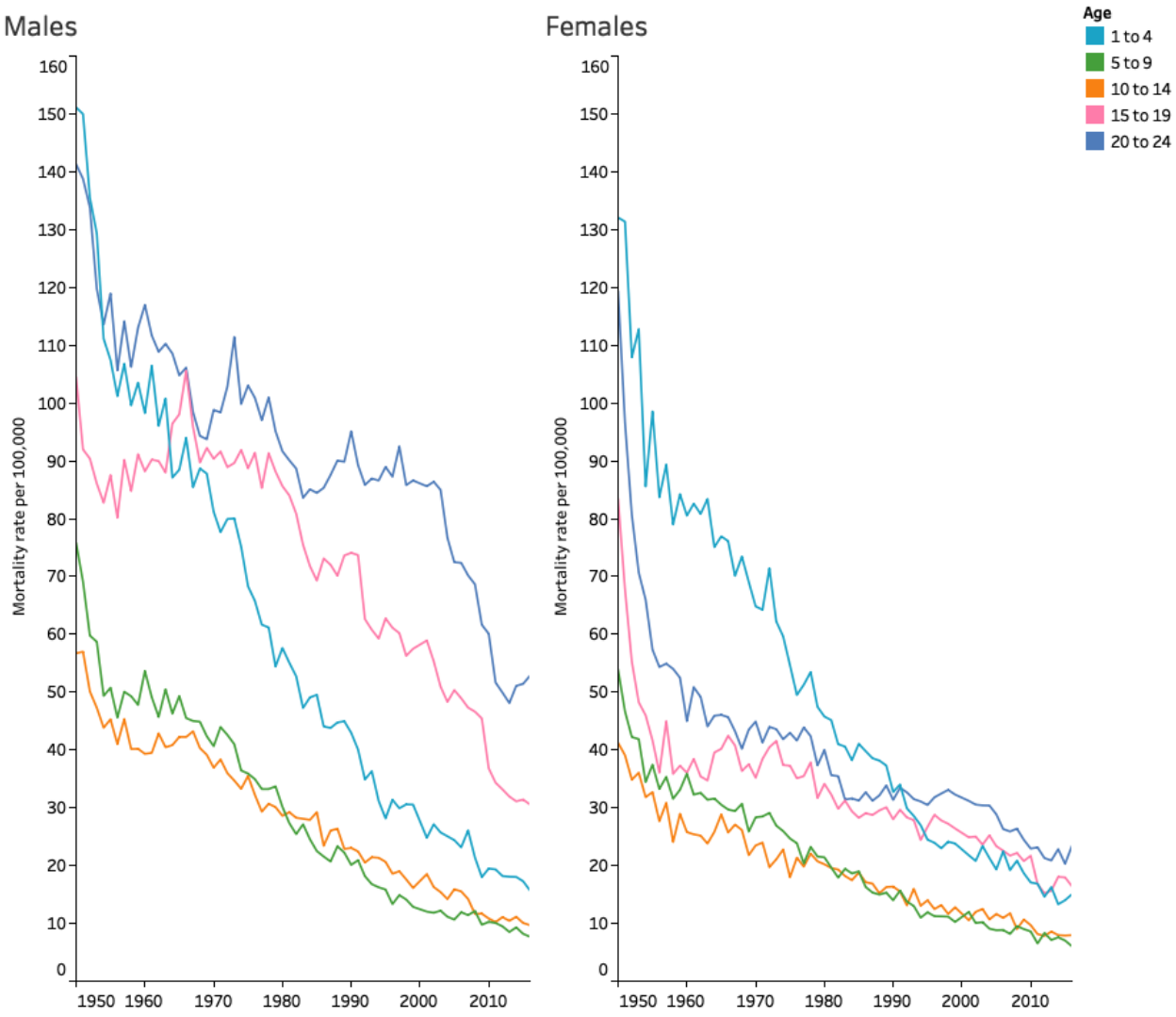


Figure 15: Proportion of CYP deaths occurring in adolescents in the UK in 1950 and 2016

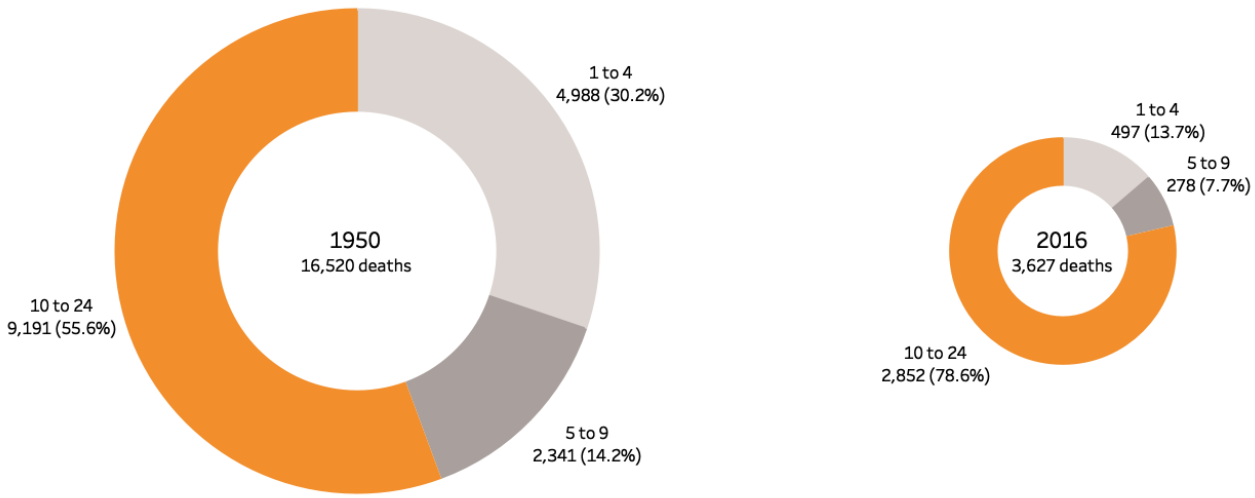
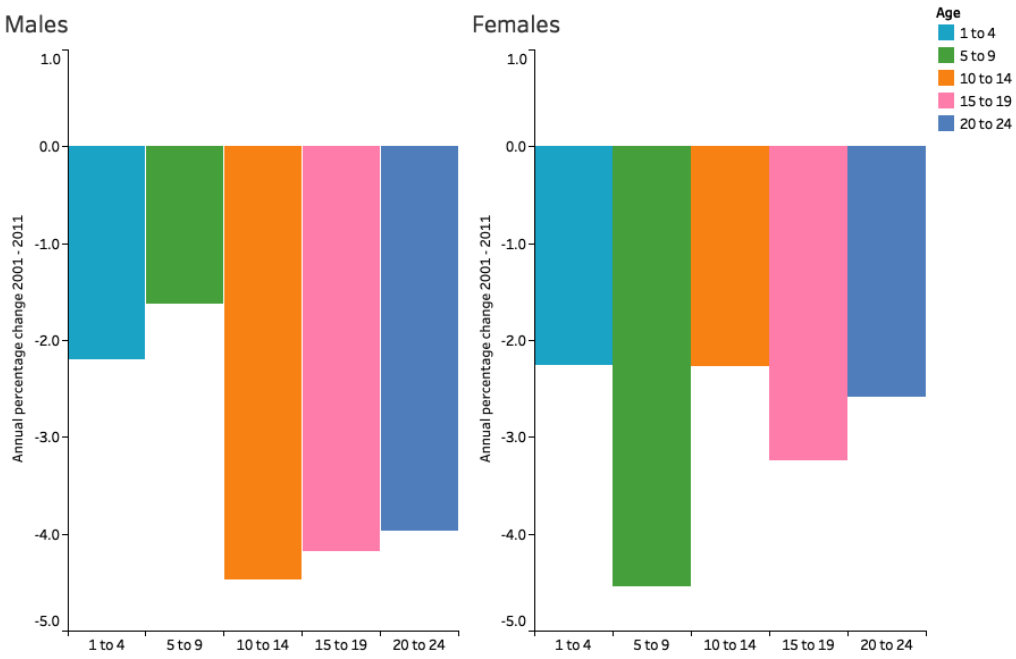
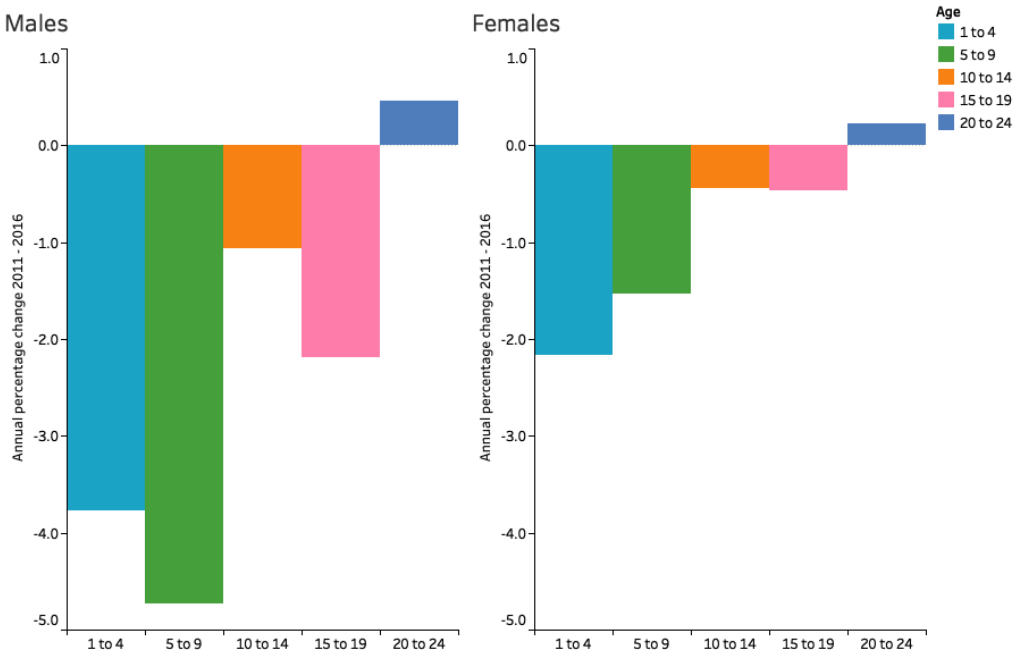


Figure 16: Annual percentage decline in mortality rate per 100,000 between 2001-2011 and 2011 -2016 by age group and sex in the UK

2001 - 2011



2011 - 2016



Trends in UK child and young person mortality by cause of death 1980 – 2017 (GBD data)

Trends in mortality rate per 100,00 by GBD cause group in 1-24 between 1980 and 2017 are shown in figures 17-21 (p.91-95), with relative change in the top 5 causes of death within each age group also shown.

Amongst 1 to 4 year olds, there have been steep declines in predominant causes of death since 1980, with similar patterns between males and females. Deaths due to injuries have shown particular improvement, with mortality rates due to transport injury reducing by around 85%. Within the top three causes of death in 2017 in this age group: mortality due to unintentional injuries have reduced by around 76%, those due to neoplasms has halved, and mortality due to the GBD group *other NCD* (of which congenital birth defects are the majority), has reduced by around 60%. Similar patterns are seen in 5 to 9, with declines in unintentional injury and transport injury (the fourth and fifth highest cause of death in this age group) of around 80% in both sexes, and deaths due to neoplasms, neurological conditions and other NCD, all reducing by more than 50% between 1980 and 2016.

Within 10 to 14, mortality due to neurological conditions (the second highest cause of death in this age group) initially increased and remained higher than in 1980 until 1998 amongst males, but by 2016 were 42.5% lower than in 1980. More modest gains were seen in females in neurological conditions, with around a 26% reduction since 1980. Although both transport and unintentional injuries have seen large declines since 1980 in both sexes, there has been very little change since 2011/12. A similar pattern was seen for other NCD in males, with the mortality rate in 2017 comparable to that in 2011.

In both males and females aged 15-24 there has been a sharp rise in deaths due to substance misuse since 1980. In 15-19, although deaths due to substance misuse have been falling sharply since around 2000, they still remain 34.7% and 65.2% higher than in 1980 in males and females respectively. In 20-24 there is a similar pattern of decline since 2000 in both sexes, but mortality rates have increased in the last 4-5years and are now 154.6% and 151.9% higher than in 1980 in males and females respectively. Mortality rates in the other leading

causes of death in 15-19 and 20-24 have seen almost no improvement since 2011/12; mortality due to self-harm has risen over the past 5 years in 20-24 in both sexes.

Figure 17: UK mortality rate per 100,000 by cause of death 1980-2017 amongst 1 to 4 year olds

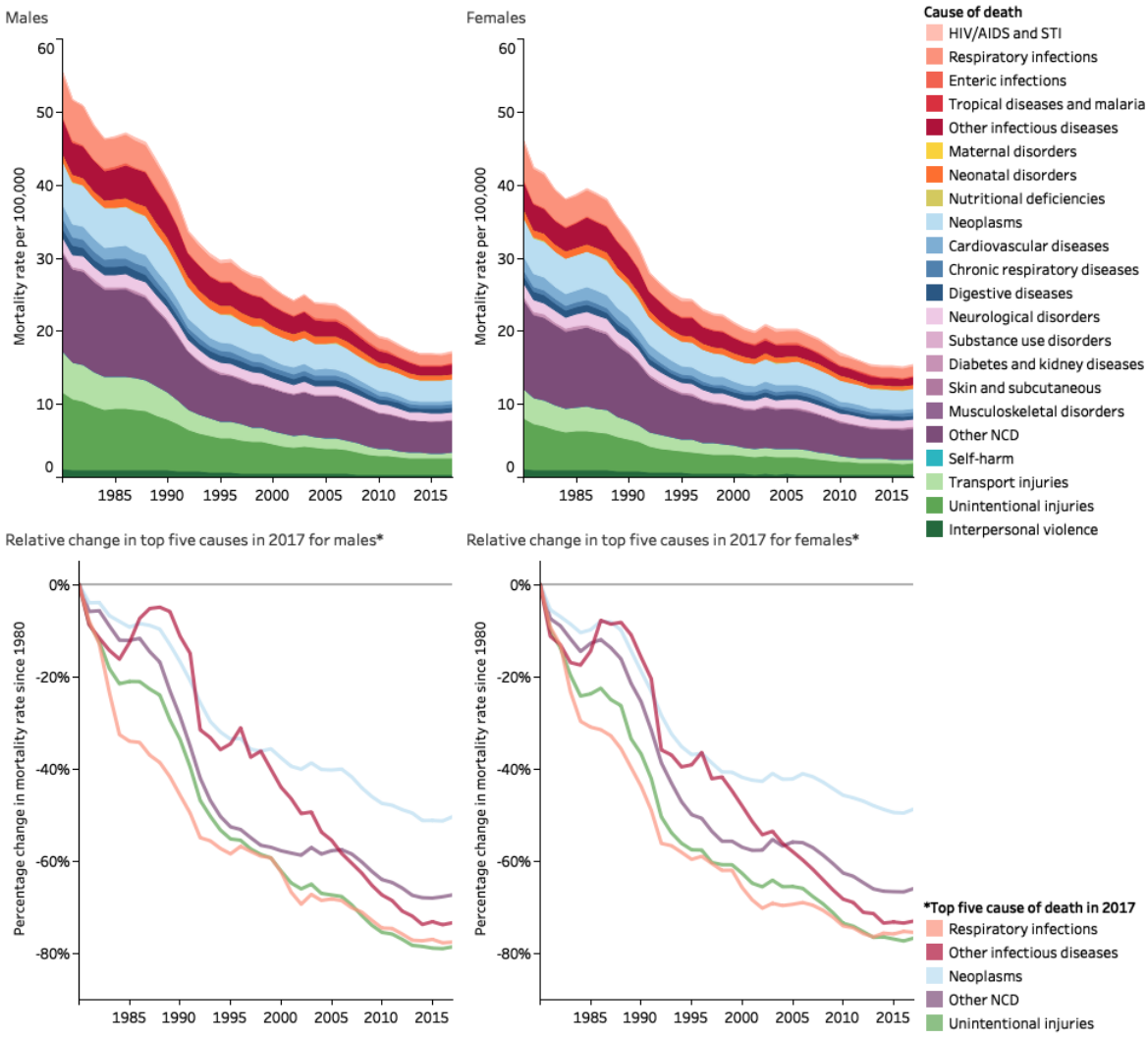


Figure 18: UK mortality rate per 100,000 by cause of death 1980-2017 amongst 5 to 9 year olds

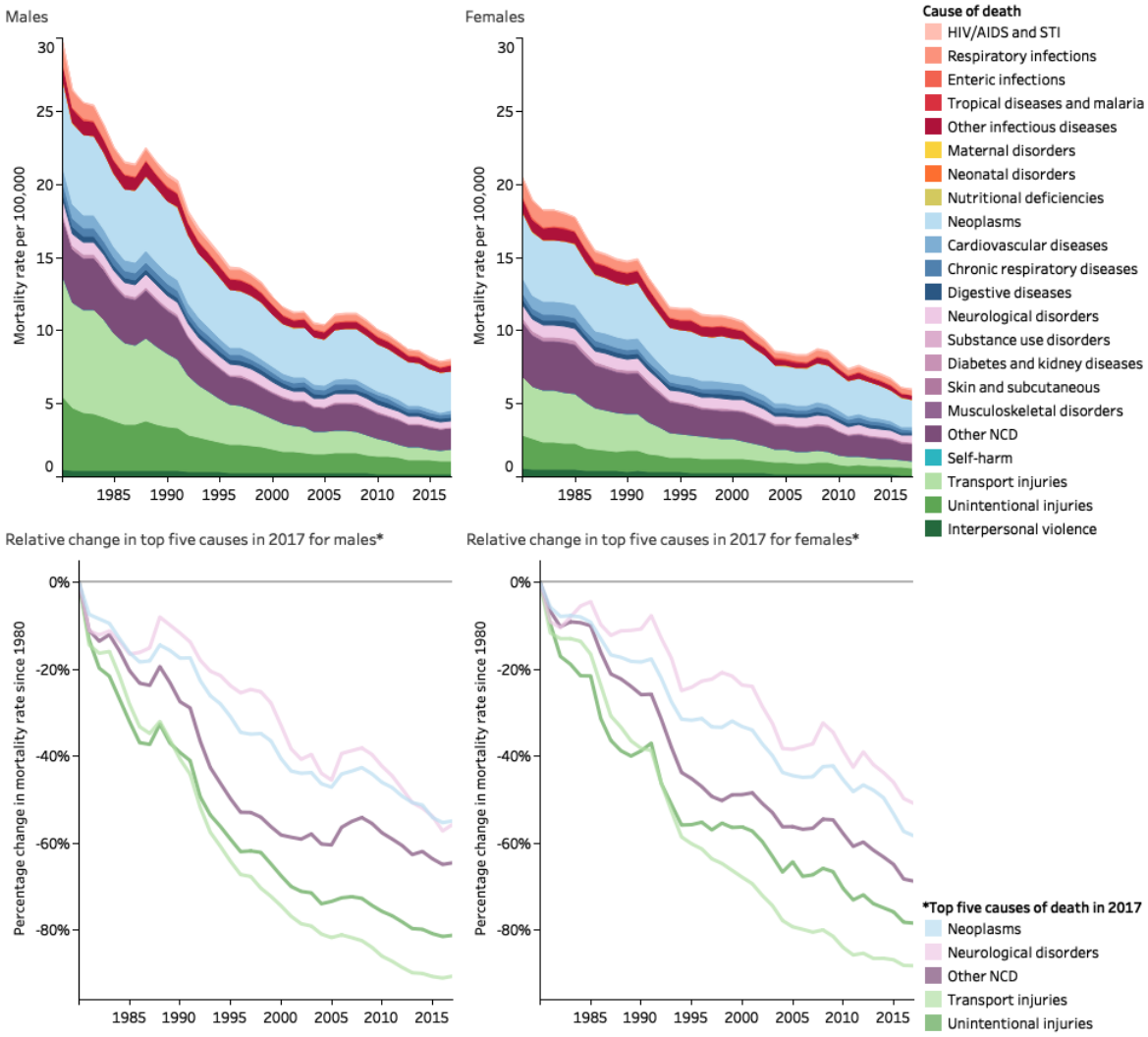


Figure 19: UK mortality rate per 100,000 by cause of death 1980-2017 amongst 10 to 14 year olds

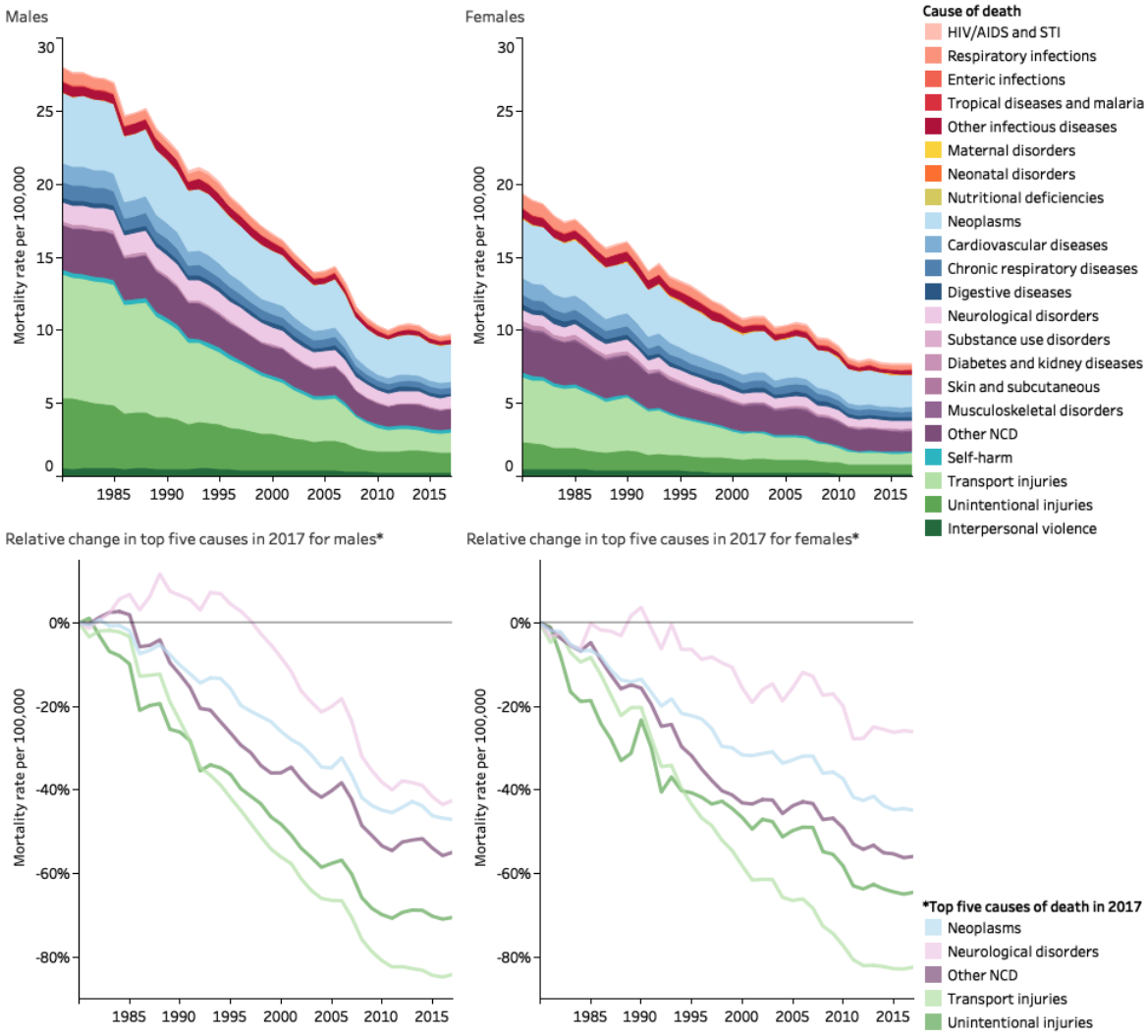


Figure 20: UK mortality rate per 100,000 by cause of death 1980-2017 amongst 15 to 19 year olds

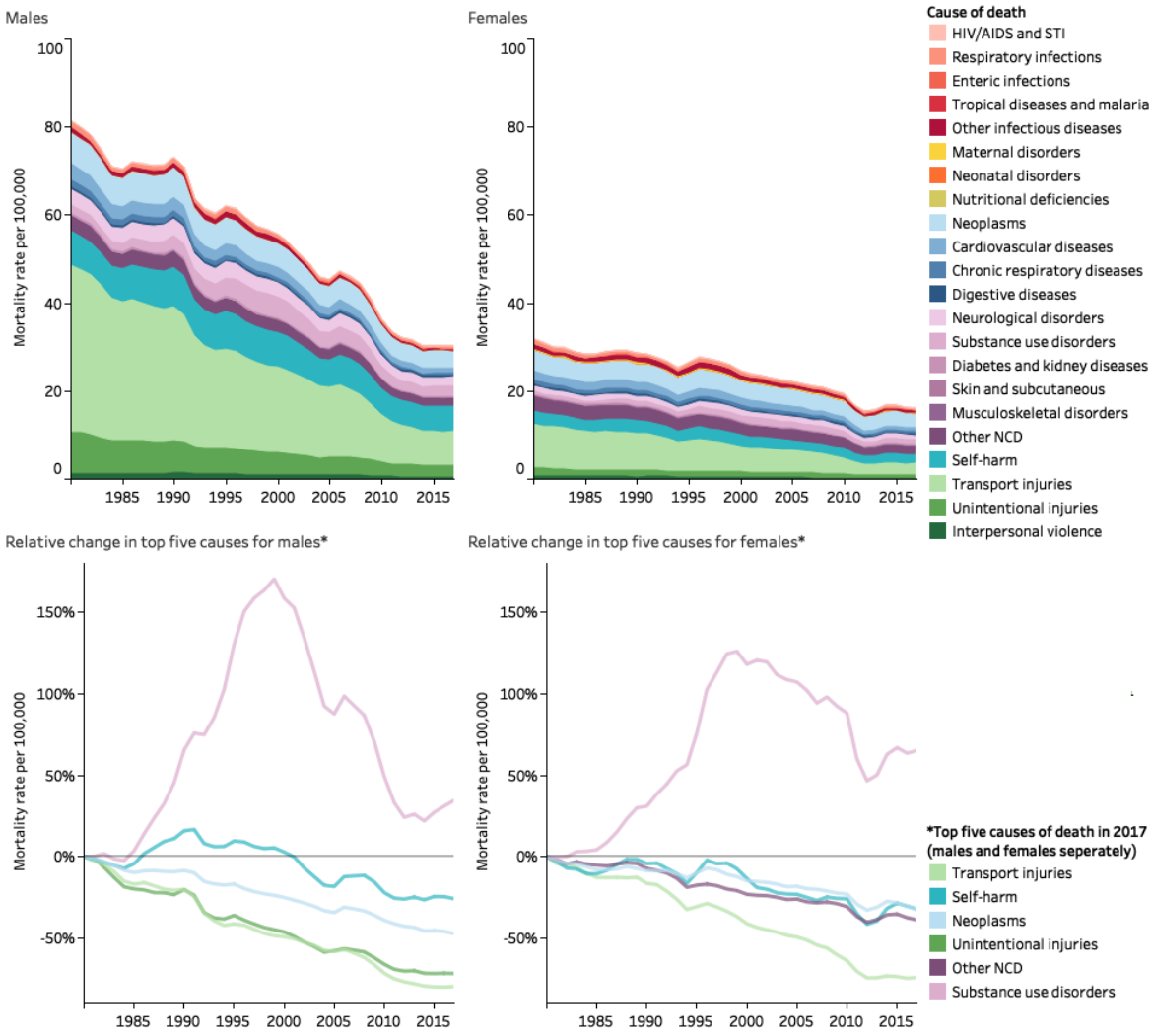
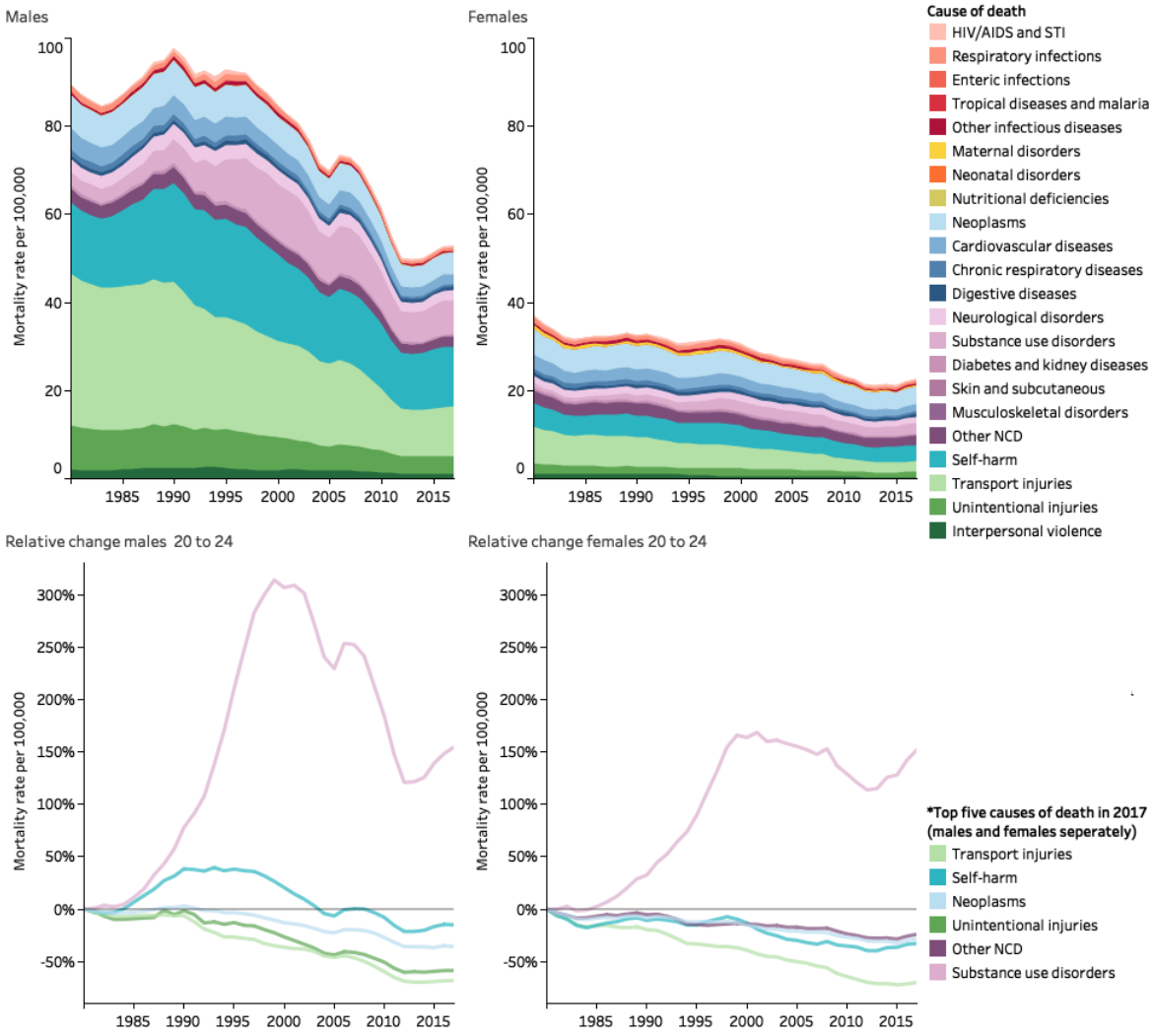


Figure 21: UK mortality rate per 100,000 by cause of death 1980-2017 amongst 20 to 24 year olds



Chapter 3 discussion

There is considerable variation in both the burden of current UK CYP mortality by age group, predominant causes of death, and both long and short terms trends over time. In 2016, amongst 1-9 the majority of deaths are spread fairly evenly between infections, neoplasms, congenital defects and injuries. Amongst adolescents 10-24 they are dominated by injuries, self-harm, and to a lesser extent, neoplasms.

Although infections still contribute to around 15% of all deaths in 1-4 year olds, these have continued to decline steeply since 1980. This likely reflects continued shifts in mortality burden away from infectious causes to non-communicable diseases and injuries seen in most high income countries (the epidemiological transition).[192] Other notable causes which have seen sharp improvements since 1980 have been to deaths due to transport injuries and other accidents, which have benefited all age groups.

Outside of infancy, most deaths during the early life course occur in adolescents and young adults, where progress in reducing mortality has been relatively slow. Although I found sharp declines in mortality in all age groups, improvements in younger age groups since 1950 have far outstripped those in late adolescence and early adulthood. As a result, more than three quarters of UK deaths in 1-24 now occur in 10-24 year olds. Of further concern is that improvements in this age groups have stagnated in recent years, and even signs of small increases in mortality amongst older adolescents and young adults. Slow recent progress in improving important causes of death in adolescents not related to injury such as self-harm, neoplasms, and some other NCDs may explain this, and aid understanding of mortality differences in the UK compared with other countries.

In this section we have described current CYP mortality burden and recent and long term trends in mortality in the UK. We will now compare these patterns with other high income countries, to identify areas which may be contributing excess UK CYP deaths.

Chapter 4

International comparisons of all-cause and cause-specific mortality in children and young people

In Chapter 2 I identified multiple studies where UK all-cause mortality for CYP has been shown to be higher than other high-income countries. However, the latest available data to highlight this was from 2014 in 0-19 year olds, and from 2008 for analyses which include 20-24 year olds. I also identified no recent studies of comparative international differences in cause specific mortality in CYP in the UK, and no previous studies examining projected trends if current differences continue. To better understand the UK's poor mortality performance, and so inform potential policy interventions to improve outcomes, a detailed assessment of recent patterns of UK CYP mortality, current burden, and forecast estimates, compared with a group of similar countries, is required.

Defining a comparator country or group of countries to benchmark the UK against is problematic. Comparisons between the UK and a single high performing country, which many authors chose to do,[19,106,107,193] can be criticised as providing the UK with unachievable targets, and potentially overlooking demographic and economic differences between countries. Using mortality within a group of similar countries can potentially provide a more stable comparator, and provide powerful policy relevant messaging. Murray et al. proposed the EU15+ as a useful comparator group for adult UK mortality in 2010.[194] The countries included were the 15 countries of the European Union (EU) prior to 2004, plus Australia, Canada, Norway and the USA. These countries were selected due to having similar underlying disease patterns and levels of healthcare expenditure to the UK. The EU15+ has subsequently used in other analyses to compare UK health outcomes internationally,[195,196] but confusingly, the list of countries included varies between studies. For example, Taib et al added New Zealand to the list proposed by Murray in one analysis of head and neck cancer survival,[197] and Gould et al. referred to the EU15+ as the pre 2004 EU countries plus Norway and Sweden in an analysis of economic growth and resilience published in 2018.[198] In other World Bank documents the EU15+ is defined as the EU15 plus Iceland, Norway and Switzerland.[199]

In 2014 Viner et al compared CYP mortality in the UK with the original EU15+ group described by Murray, but excluded the USA due to its high child and infant mortality and large differences between health system factors compared with the UK.[17] Further studies using this definition have cemented this selection of countries a useful comparator group for UK CYP mortality,[14,105] which I have also adopted for this analysis. The list of countries included in this definition for the EU15+ are: Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, Australia, Canada, and Norway.

In this chapter I will compare UK CYP mortality with the EU15+ in three parts. First, I will use mortality estimates provided by the World Health Organization World Mortality Database (WMD) to compare CYP mortality (1-24) outcomes in the UK with the EU15+ for between 1970 and 2016 for all causes of death. Secondly, I will identify the causes of death which are contributing most to current differences in mortality between the UK and EU15+, again using WHP WMD data. Finally, I will use data provided by the Institute of Health Metrics and Evaluation (IHME) to describe forecast all-cause mortality trends in the UK and the EU15+ from 2016 – 2040, to highlight likely future excess UK CYP mortality.

The sections of this chapter relating to current cause specific differences in UK CYP mortality compared with the EU15+ has contributed to the following publications:

Ward JL, Wolfe I, Viner RM Cause-specific child and adolescent mortality in the UK and EU15+ countries *Arch Dis Child* 2020

Viner R, **Ward J,** Cheung R, Wolfe I, Hargreaves D. Child health in 2030 in England: comparisons with other wealthy countries *RCPCH* 2018

Chapter 4 methods

Data

WHO World Mortality Data

All-cause and cause specific mortality estimates for children and young people 1-24 in the UK, and countries of the EU15+, were provided by the WHO World Mortality Database (WMD). Cause specific estimates were accessed on 9th Oct 2017 from (http://www.who.int/healthinfo/mortality_data/en/). I then examined all-cause trends accessing data on 19th December 2019 (after the cause-specific analyses had been submitted for publication).[95]

National mortality estimates were available for the UK and EU15+ countries by cause, year, sex and 5-year group (1-4, 5-9, 10-14, 15-19 and 20-24). I limited all-cause analyses to years 1970 – 2016, due to variable data availability for EU15+ countries prior to this.

At the time I downloaded cause specific data, estimates for the UK were available to 2016, however only 11 EU15+ countries had data this recent. I subsequently used data from 2015 to assess cause specific differences, where data were available within 1 year for 16/17 EU15+ countries. I limited the cause-specific analysis to country-years using ICD10 codes to improve comparability between countries and over time. I used the methods described in Chapter 2 to categorize causes of death to 22 cause groups and redistribute inappropriately coded deaths ("garbage codes").[200]

Forecast data and the Global Burden of Disease study

As part of the Global Burden of Disease Study 2016, the Institute of Health Metrics and Evaluation (IHME) developed forecast mortality estimates for 195 countries to 2040.[201] These attempt to expand previous models to predict life-expectancy or age specific mortality which use time as the only independent variable. In place of this approach, IHME uses predicted change in drivers of specific causes of mortality, population exposure to certain risk factors and interventions, and change in indicators of country development, to forecast cause-specific mortality estimates by age group, location and sex. Estimates for all-cause mortality

are then calculated as the sum of cause specific estimates. The GBD forecasting model use estimates for the prevalence of 65 risk factors (for example vaccination, smoking, air pollution, and met contraception need) and relative risks for death according to different levels of these exposures based on metanalyses of previous studies.[202] Their model then incorporates variation in mortality reflected in country sociodemographic index (SDI), a summary indicator of three components strongly associated with health outcomes. SDI has evolved through iterations of the GBD, but as used in GBD 2016 (on which forecast data are based) is calculated using index values for income per capita, mean years of education, and total fertility under 25 for each location-year.[1] Finally, the model captures variation over time not explained by SDI, risk factors or interventions included in the components above. Forecasts for each driver for mortality then contribute to overall predicted cause-specific and all-cause mortality. Full details of the models used to develop these estimates are provided by Foreman et al.[201]

GBD forecast mortality estimates are publicly available, and I downloaded data for the UK and EU15+ countries from 2016 – 2040 from the Global Burden of Disease 2016 Foresight Visualization suite on 29th June 2020 here http://www.healthdata.org/data-visualization/gbd-foresight-visualization. Data were available for all-cause mortality rate per 100,000 population in 1-4, 5-9, 10-14, 15-19 and 20-24 year old by sex.[201]

Procedures

I first examined all-cause and cause specific differences in CYP mortality in the UK compared with the EU15+, using WHO WMD data. To account for the large annual variation in mortality for some causes, I first calculated lagged three year mean number of deaths and mortality rate per 100,000 for all causes of death, and then each cause, age group, sex and country-year available.

All-cause mortality differences

I then compared the three-year lagged mean mortality rate for all-causes of death in the UK with the best performing EU15+ country, and then the EU15+ 50th (median), and EU15+ 25th and EU15+ 75th centile, by age group and sex between 1970 and 2016. I did this by calculating

the percentage difference between the UK and EU15+ median, 25th and 75th centile estimate, and describe how this has changed between 1970 and 2016. I used the 25th, 50th (median) and 75th centile EU15+ mortality as comparators to the UK estimate to provide context as to how the UK compares to the average, upper or lower quartile EU15+ country for mortality by sex and age group. I then calculated the number of deaths which would have been avoided had UK outcomes been similar to the best performing country, by using the lowest EU15+ mortality rate, and population estimates for the UK, within in each age and sex group. Due to its small population size, Luxembourg was excluded when comparing UK outcomes with the best performing EU15+ countries.

Cause-specific mortality differences

I then examined recent cause specific differences in CYP mortality in the UK and EU15+ using cross-sectional poisson regression models. I chose to use poisson regression in these analyses as data were of counts of deaths, and I did not find evidence for over-dispersion, where negative binomial models may have been more appropriate (likelihood ratio test of alpha >0.05).

I calculated incident rate ratios (IRR) with 95% confidence intervals to compare the three-year lagged mean number of deaths in the UK with all 17 EU15+ countries in 2015, for each cause amongst 1-4, 5-9, 10-14 and 15-19 and 20-24 year olds. I excluded causes which contributed to less than 1% of all deaths in that age/sex group. If countries did not have data for 2015, I used the three-year lagged mean number of deaths prior to the latest available data year. I was unable to use lagged mean estimates for Greece, as data were only available for 2014. I used mid-year population denominators provided by the WMD as an offset in each model (meaned over the same 3-year period as number of deaths). Where population data were not available from the WMD I used estimates provided by national statistics databases. As patterns of cause of death are similar during early childhood (1-9), but with large differences during adolescence, I present results for both sexes for 1-4 and 5-9 year olds, and by sex for 10-14, 15-19 and 20-24 year olds. Due to concerns regarding the high proportion deaths which were redistributed, I performed a sensitivity analysis repeating the procedures described above but excluding all garbage coded deaths.

To account for multiple testing within each cause group, I defined significant differences in mortality between the UK and EU15+ as $p< 0.005$, approximating to a Bonferroni correction but avoiding different thresholds for significance within each cause, sex, age group. Where there were significant mortality differences between the UK and EU15+ for a cause, I used UK age and sex specific population estimates to calculate number of deaths if UK mortality rates were similar to the EU15+ median (i.e. the average) and EU15+ 10^{th} centile (i.e. the best 10%). For causes where the EU15+ 10^{th} centile for mortality was zero, I used the lowest non-zero national mortality rate.

I then ranked the UK compared with EU15+ countries using the three-year lagged mean mortality rate per 100,000 in 2015 (or latest date available) and 2010. I then show the UK's current position and change in rank from 2010 to 2015. Greece was excluded from the ranking analysis as data were only available for one year (2014).

Forecast all-cause mortality differences

Finally, I examined projected CYP mortality in the UK for all causes compared with the EU15+ median, 25^{th} and 75^{th} centile, using similar methods to those used in describing trends between 1970-2016. I did this by comparing predicted percentage change in mortality in the UK and EU15+ median between 2016 and 2040. I then calculated the percentage difference between in the UK and EU15+ median mortality rate in 2016 and the projected value for 2040, by age group and sex. All analyses were performed in Stata 14 (StataCorp, College Station TX).

Chapter 4 results

UK all-cause mortality compared with the EU15+ 1970 – 2016

In 2016, the EU15+ country with the lowest three year lagged mean mortality rate for 1-24 year olds was the Netherlands amongst males (18.95 per 100,000) and Norway amongst females (11.49 per 100,000). If the UK had similar outcomes, there would be around 728 fewer deaths each year in the UK, or around 2 a day. However, mortality performance differs by age within countries, with Scandinavian countries having the best outcomes for 1-14 year olds, but perform worse for 15-24 year olds. Had the UK had the best mortality rate amongst EU15+ countries within each age and sex group in 1-24 year olds, around 1000 deaths would be avoided each year.

Figures 22-26 (p.104-108) show the three-year lagged mean mortality rate in the UK amongst 1-24 compared with the EU15+ median, 25th and 75th centile, from 1970 – 2016, and the percentage difference between the UK estimate and the EU15+ median over this time. The UK mortality rate was lower than the EU15+ median in all 5-year groups in 1970. By 2016 mortality rates in the UK were higher than the EU15+ median in all 5-year age groups and both sexes except males 20-24.

Amongst 1 to 4 year olds, UK outcomes were around 15% lower than the EU15+ median in both sexes in 1970, and are now 5% higher amongst males and 15% higher amongst females. Amongst 5 to 9 year olds, outcomes in both sexes were around 20% lower than the EU15+ median in 1970, but were equivalent in 2016. Amongst 10-14 year olds, mortality rates in the UK were around 17% lower than the EU15+ median in 1970; in 2016 the mortality rate amongst males was around 10% higher and amongst females equivalent to the EU15+ median. Similar trends were seen in mid adolescence and young adults, where mortality in the UK is now around 14% higher than the EU15+ median in females, and equivalent to the EU15+ median amongst males. Amongst 20-24, mortality rates amongst females were around 20% lower than the EU15+ median in 1970 and are now 10% higher, and in males were 30% lower in 1970 and are now around 5% lower.

Figure 22: UK mortality rate per 100,000 in 1 to 4 compared with the EU15+ median 1970 – 2016

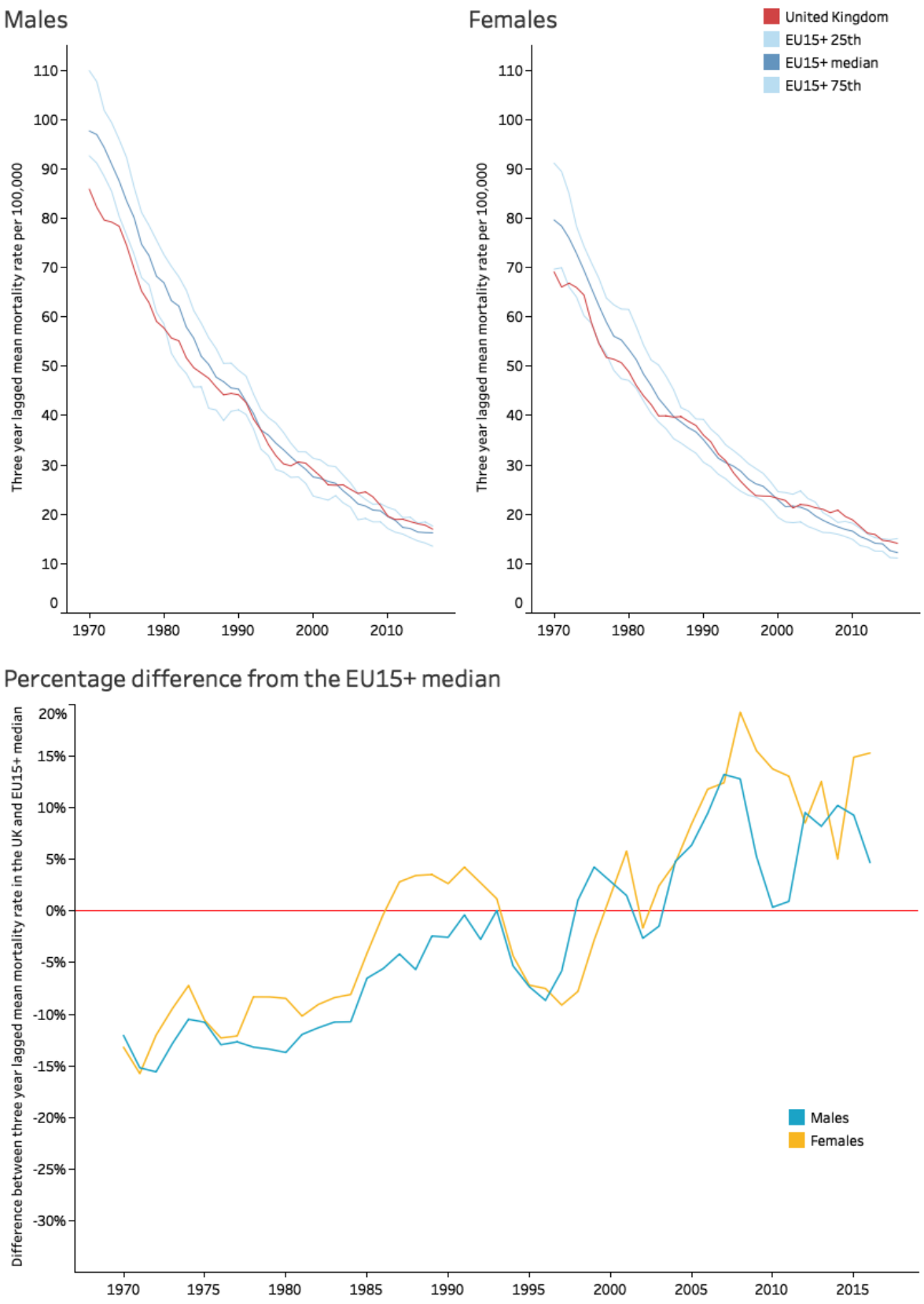


Figure 23: UK mortality rate per 100,000 in 5 to 9 compared with the EU15+ median 1970 – 2016

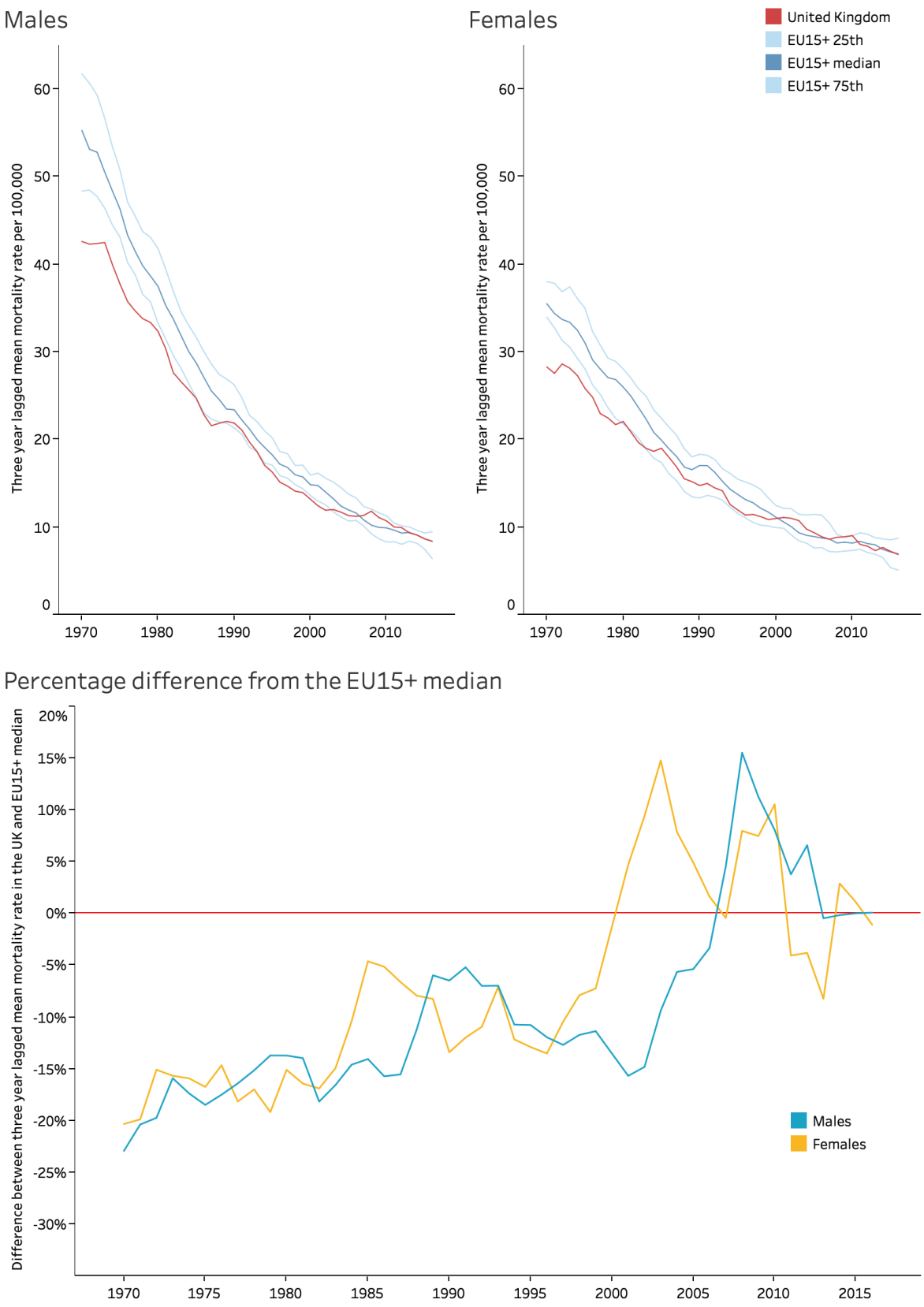


Figure 24: UK mortality rate per 100,000 in 10 to 14 compared with the EU15+ median 1970 – 2016

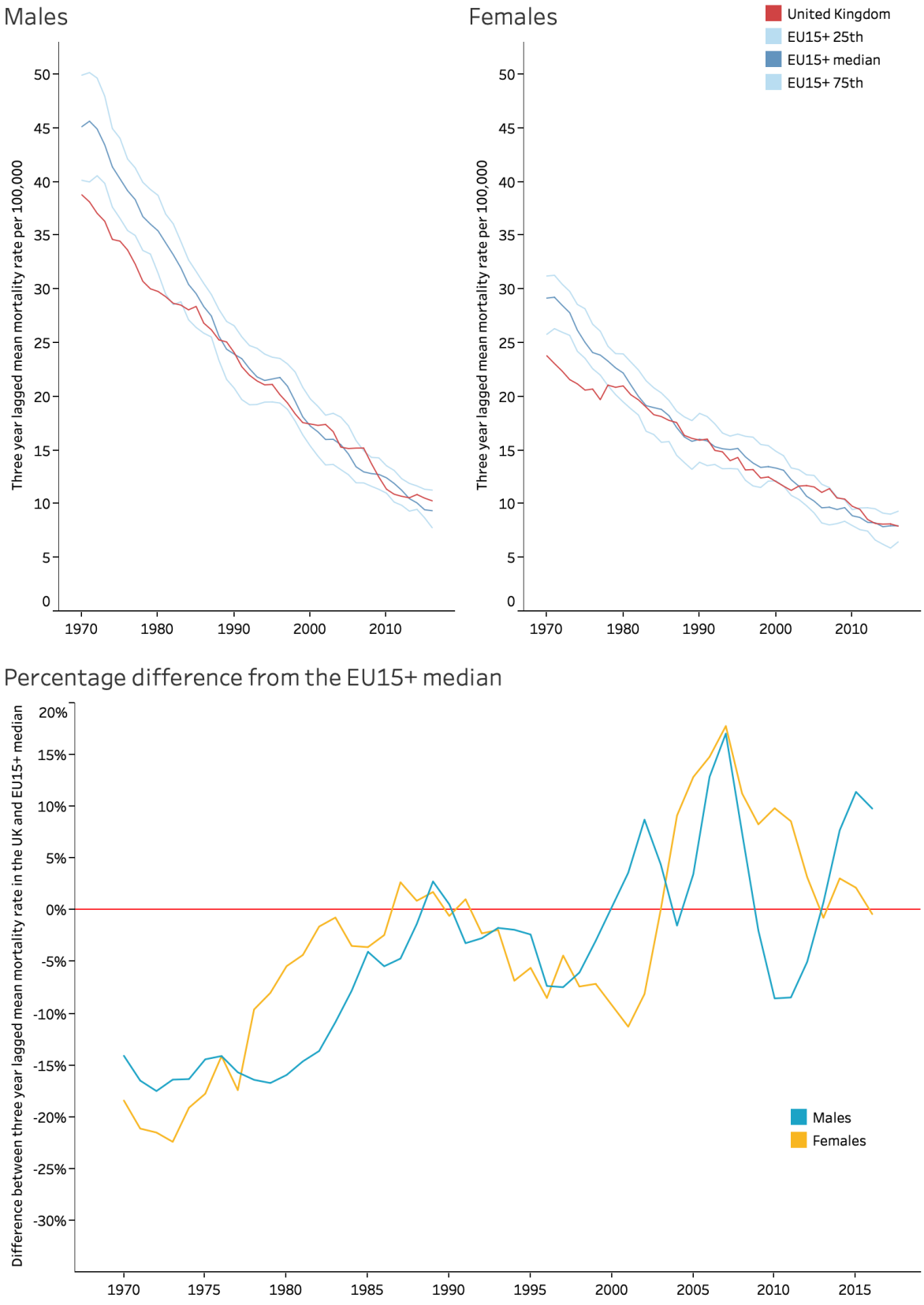
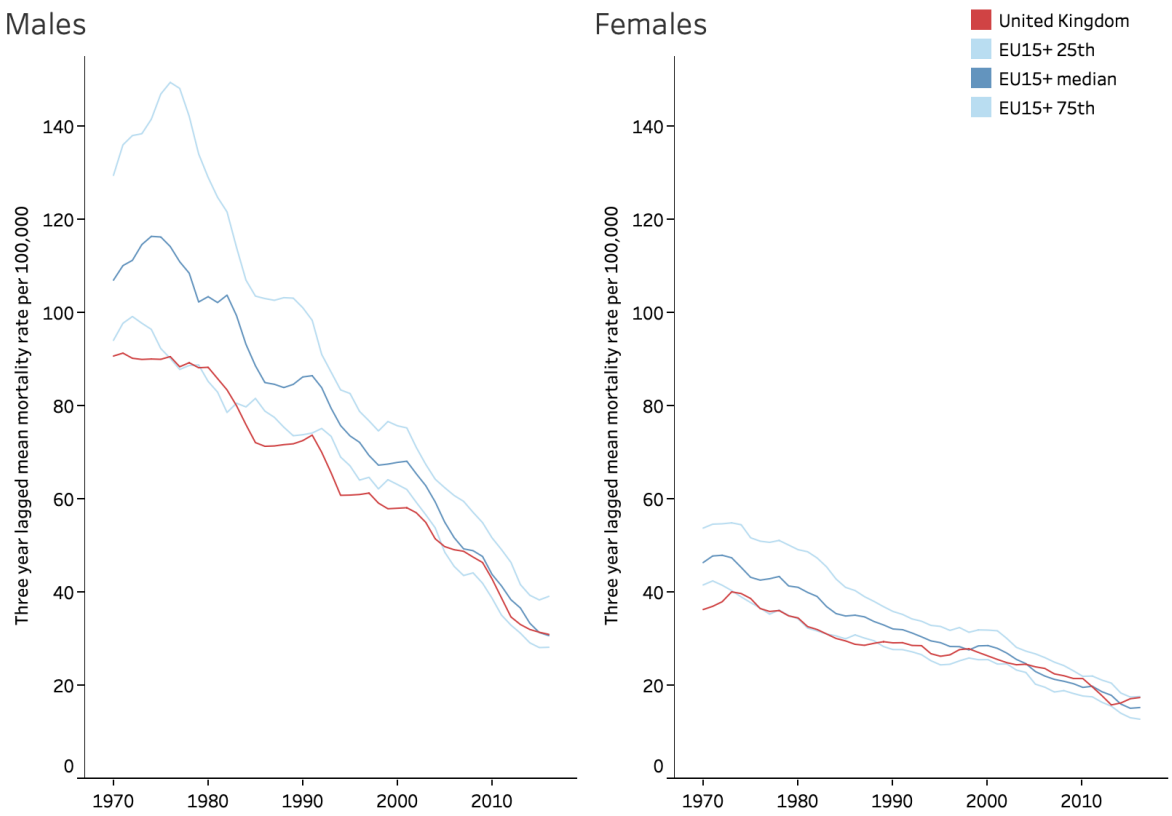


Figure 25: UK mortality rate per 100,000 in 15 to 19 compared with the EU15+ median between 1970 – 2016



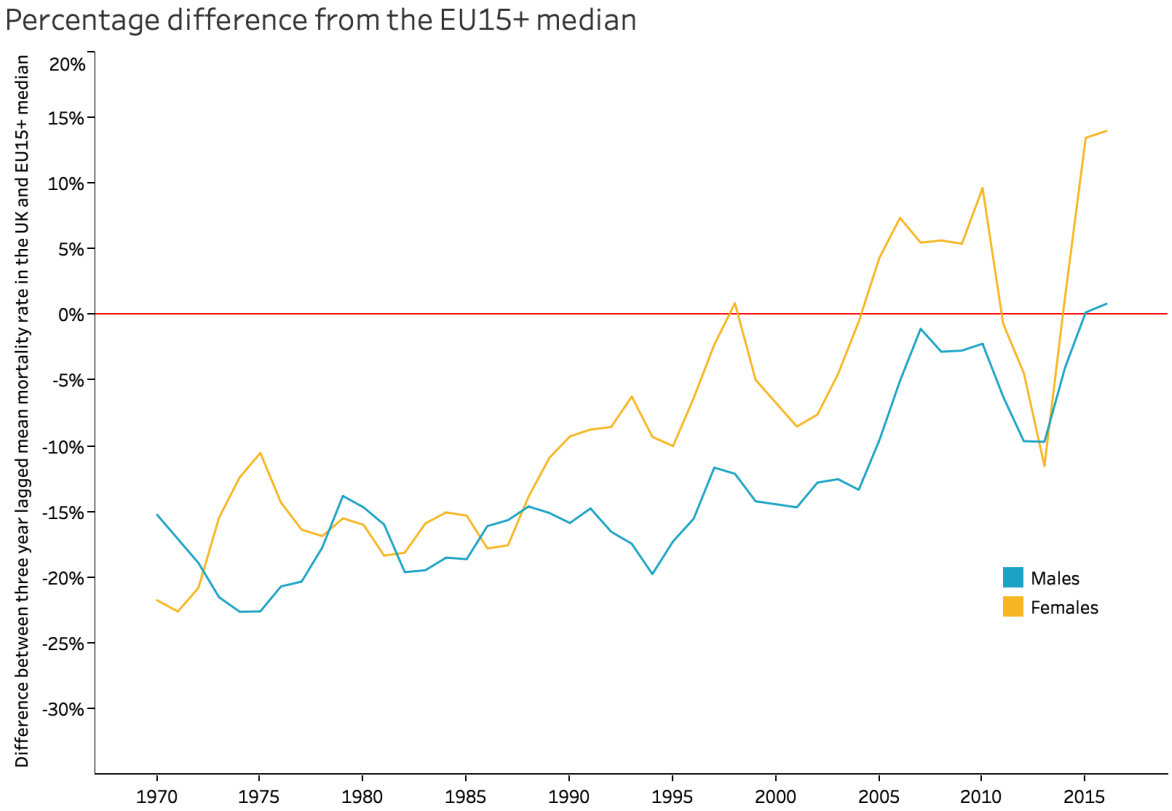


Figure 26: UK mortality rate per 100,000 in 20 to 24 compared with the EU15+ median between 1970 – 2016

Recent cause specific differences in child and young person mortality in the UK compared with the EU15+

The three-year lagged mean number of deaths in children and young people 1-19 in 2015 in the UK was 2110 (1281 males and 829 females). NCD causes made up the greatest proportion of UK deaths in early childhood (1-9) and for adolescent females (10-19), with injury causes accounting for the greatest number of deaths in adolescent males. Communicable diseases were the least common cause of death in all age groups except 1-4 year olds, where they accounted for between 19 – 21% of all deaths.

In the UK, common infections accounted for the greatest proportion of deaths within the communicable cause group (more than 80%), and neoplasms were the most common NCD cause (between 28 and 43%), in males and females in both age groups. Within injury causes, unintentional injuries were the most common cause in 1-4 year olds, with transport injuries the most common cause in all other age groups except males 15-24 and females 20-24 where 24 where self-harm was the leading cause of death.

Tables 6-9 (p.112) show the three year lagged mean annual number of deaths in the UK in 2015 and the proportion of total mortality, for 1-4 and 5-9 (both sexes) and 10-14, 15-19 and 20-24 by sex. The incidence rate ratio (IRR) for UK mortality compared with EU15+ countries is also shown, with 95% confidence intervals. Significant ($p<0.005$) differences in mortality are highlighted in red. The UK had significantly higher mortality for common infections in 1-4 and 5-9 year olds (both sexes), 10-14 year olds males and 15-19 year olds females, and for chronic respiratory conditions in 5-9 and 10-14 year olds in both sexes. The UK also had significantly higher mortality than the EU15+ for neurological disorders and diabetes/urological/blood/endocrine disorders (DUBE) in 15-19 females and 20-24 males, and for digestive conditions in 15-19 females. UK mortality was significantly lower than the EU15+ for transport injuries amongst males 15-24, females 20-24, and for interpersonal violence in males 20-24.

Table 10 (p.116) shows most recent UK mortality rank compared to the other EU15+ countries (excluding Greece) using the latest mortality rate per 100 000 estimate available for each country (meaned over the previous 3 years), for males and females. In order to demonstrate

the UK's position relative to other EU15 countries, cells in this table are shaded green (lowest mortality) to yellow (median mortality) to red (highest mortality). The UK ranked 16th or 17th (highest or second highest mortality) for common infections across all age groups in and both sexes. The UK ranked 14th-17th for chronic respiratory diseases in males and females in all age groups, and in the bottom 5 countries for most other NCD mortality groups except neoplasms. All causes of injury mortality in the UK were ranked in the top 10 countries in males and females for all age groups except transport injuries in males 10-14 (11th) and unintentional injuries in 20-24 in females (11th).

Results from the sensitivity analyses showed a similar pattern of mortality differences between the UK and EU15+. After excluding redistributed deaths, the UK still had significantly higher mortality for common infections in 1-4 (both sexes), chronic respiratory diseases in 10-14 (both sexes), and neurological conditions in 15-19 females. The UK had significantly lower mortality than the EU15+ for transport injuries in 15-19 males, unintentional injuries in 1-4 (both sexes) and self-harm in 15-19 females. The IRR for other age/cause groups identified in the main analysis as having higher mortality in the UK compared to the EU15+ were similar in the sensitivity analysis, but no longer reached significance using the reduced number of deaths.

Table 11 (p.117) shows change in UK mortality rank from 2010 to latest available estimate. Cells are shaded green if the UK's rank has improved by more than 2 places since 2010, and red if it has worsened by more than 2 places since 2010. For common childhood infections (which accounted for >80% of deaths within communicable/maternal conditions) there has been little change since 2010 for the UK's mortality rank in males or females across all age groups. Within NCDs the UK has dropped more than 2 ranking places compared with the EU15+ in neoplasms (both sexes 1-4 and females 20-24), cardiovascular diseases (both sexes 1-4, females 10-14 and females 20-24), chronic respiratory diseases (males 15-19) and DUBE (males 10-14). The UK position has however improved for some causes, notably neoplasms where the UK position has improved between 4 to 5 places for 5-9 year olds, 10-14 year olds females and 15-19 year old males. Within injuries, there were large improvements in mortality rank for males 5-9, where transport injuries improved 8 places. However, the UK

dropped more than 2 ranking places for self-harm (10-14 and 15-19 males), interpersonal violence and unintentional injury (10-14 and 20-24 males)

Table 6: Incidence rate ratio (IRR) with 95% confidence intervals for three year lagged mean number of deaths in UK compared with EU15+ in 2015[i] for 1-4 and 5-9 year olds (both sexes)

	Both sexes 1 to 4						Both sexes 5 to 9					
	Deaths[ii]	% of total	IRR	p	lower CI	upper CI	Deaths[ii]	% of total	IRR	p	lower CI	upper CI
Communicable / neonatal												
Common infections	85	16.2	2.08	<0.001	1.61	2.67	25	8.0	2.38	<0.001	1.48	3.83
Neonatal disorders	11	2.1	1.45	0.28	0.74	2.85	3	1.0	1.12	0.86	0.32	3.90
Other communicable	7	1.3	2.27	0.07	0.92	5.56						
Non-communicable diseases												
Neoplasms	93	17.8	0.94	0.58	0.75	1.17	106	34.4	0.91	0.34	0.74	1.11
Cardiovascular diseases	23	4.4	1.22	0.40	0.77	1.91	13	4.4	1.26	0.45	0.69	2.28
Chronic respiratory diseases	13	2.4	1.76	0.08	0.93	3.31	14	4.4	3.25	<0.001	1.66	6.37
Digestive diseases	11	2.0	1.85	0.09	0.91	3.74	9	2.8	2.52	0.02	1.12	5.65
Neurological disorders	50	9.5	1.23	0.20	0.90	1.67	19	6.2	0.87	0.56	0.53	1.40
DUBE[iii]	52	9.9	1.01	0.94	0.75	1.36	28	9.1	1.12	0.60	0.74	1.68
Other NCD	87	16.5	1.00	0.99	0.79	1.26	38	12.4	1.26	0.20	0.89	1.79
Injuries												
Transport injuries	23	4.4	0.60	0.02	0.39	0.93	23	7.5	0.68	0.08	0.44	1.05
Unintentional injuries	58	11.0	0.71	0.01	0.54	0.94	18	6.0	0.56	0.02	0.35	0.90
Interpersonal Violence	6	1.2	0.46	0.06	0.20	1.02	4	1.4	0.53	0.21	0.20	1.44

Causes contributing to less than 1% of total deaths are not shown. Causes where there were significant differences in mortality between the UK and EU15+ are highlighted in red.

[i] For EU15+ countries without data to 2015, I used lagged mean number of deaths over the three years prior to the latest available data year in poisson regression models for all countries except Greece, where data were only available for 2014. [ii] Mean annual number of deaths between 2013 and 2015 in the UK. [iii] Diabetes, urogenital, blood, endocrine disorders.

Table 7: Incidence rate ratio (IRR) with 95% confidence intervals for three year lagged mean number of deaths in UK compared with EU15+ in 2015[i] for 10-14 year olds by sex

	Males 10 to 14						Females 10 to 14					
	Deaths[ii]	% of total	IRR	p	lower CI	upper CI	Deaths[ii]	% of total	IRR	p	lower CI	upper CI
Communicable / maternal												
Common infections	12	6.3	3.02	<0.001	1.51	6.06	6	4.6	1.75	0.21	0.73	4.21
Non-communicable diseases												
Neoplasms	52	27.2	0.94	0.68	0.70	1.26	36	25.9	0.80	0.21	0.57	1.13
Cardiovascular diseases	11	5.9	1.24	0.52	0.65	2.35	8	5.6	1.10	0.81	0.51	2.36
Chronic respiratory diseases	11	5.7	3.65	<0.001	1.72	7.77	9	6.7	4.29	<0.001	1.85	9.95
Digestive diseases	3	1.6	2.45	0.18	0.66	9.15	4	3.2	3.87	0.03	1.17	12.77
Neurological disorders	13	6.7	1.13	0.69	0.62	2.05	12	8.2	1.26	0.47	0.67	2.38
DUBE[iii]	14	7.5	1.25	0.45	0.70	2.20	15	10.9	1.34	0.31	0.77	2.32
Other NCD	15	7.8	1.03	0.91	0.59	1.79	16	11.7	1.12	0.68	0.66	1.89
Injuries												
Transport injuries	30	15.8	1.04	0.85	0.70	1.53	13	9.3	0.79	0.42	0.44	1.41
Unintentional injuries	15	7.9	0.87	0.62	0.51	1.50	8	5.3	0.96	0.91	0.44	2.07
Self harm	10	5.2	0.56	0.08	0.29	1.06	9	6.7	0.61	0.15	0.31	1.19
Interpersonal Violence	2	1.0	0.61	0.52	0.14	2.74	2	1.2	0.51	0.41	0.10	2.54

Causes contributing to less than 1% of total deaths are not shown. Causes where there were significant differences in mortality between the UK and EU15+ are highlighted in red.

[i] For EU15+ countries without data to 2015, I used lagged mean number of deaths over the three years prior to the latest available data year in poisson regression models for all countries except Greece, where data were only available for 2014. [ii] Mean annual number of deaths between 2013 and 2015 in the UK. [iii] Diabetes, urogenital, blood, endocrine disorders.

Table 8: Incidence rate ratio (IRR) with 95% confidence intervals for three year lagged mean number of deaths in UK compared with EU15+ in 2015[i] for 15-19 year olds by sex

	Males 15-19						Females 15-19					
	Deaths[ii]	% of total	IRR	p	lower CI	upper CI	Deaths[ii]	% of total	IRR	p	lower CI	upper CI
Communicable / maternal												
Common infections	15	2.5	2.14	0.01	1.19	3.86	17	5.3	2.91	<0.001	1.62	5.21
Non-communicable diseases												
Neoplasms	81	13.1	0.94	0.60	0.74	1.19	63	19.6	1.04	0.75	0.80	1.37
Cardiovascular diseases	29	4.7	1.18	0.43	0.79	1.75	16	5.0	1.18	0.54	0.69	2.02
Chronic respiratory diseases	8	1.3	1.54	0.28	0.70	3.37	8	2.6	2.68	0.02	1.17	6.09
Digestive diseases	7	1.1	2.19	0.08	0.90	5.32	8	2.6	3.60	0.0041	1.50	8.62
Neurological disorders	43	6.9	1.60	0.01	1.14	2.25	27	8.4	2.02	0.002	1.30	3.12
DUBE[iii]	30	4.7	1.74	0.01	1.15	2.62	30	9.4	1.81	0.0045	1.20	2.72
MSK[iv]							4	1.4	3.42	0.04	1.05	11.12
Other NCD	16	2.6	0.85	0.54	0.50	1.43	18	5.5	1.15	0.58	0.69	1.93
Injuries												
Transport injuries	152	24.4	0.70	<0.001	0.59	0.83	57	17.8	0.77	0.07	0.59	1.02
Unintentional injuries	53	8.5	0.92	0.56	0.69	1.23	13	4.1	1.05	0.87	0.59	1.89
Self harm	168	27.0	1.05	0.55	0.89	1.24	51	15.7	0.70	0.02	0.52	0.94
Interpersonal Violence	8	1.2	0.46	0.04	0.22	0.96						

Causes contributing to less than 1% of total deaths are not shown. Causes where there were significant differences in mortality between the UK and EU15+ are highlighted in red. [i] For EU15+ countries without data to 2015, I used lagged mean number of deaths over the three years prior to the latest available data year in poisson regression models for all countries except Greece, where data were only available for 2014. [ii] Mean annual number of deaths between 2013 and 2015 in the UK. [iii] Diabetes, urogenital, blood, endocrine disorders.

Table 9: Incidence rate ratio (IRR) with 95% confidence intervals for three year lagged mean number of deaths in UK compared with EU15+ in 2015[i] for 20-24 year olds by sex

	Males 20-24						Females 20-24					
	Deaths[ii]	% of total	IRR	p	lower CI	upper CI	Deaths[ii]	% of total	IRR	p	lower CI	upper CI
Communicable / maternal												
Common infections	23	2.09	1.63	0.08	0.95	2.80	15	3.54	2.01	0.02	1.12	3.60
Non-communicable diseases												
Neoplasms	109	9.69	0.82	0.05	0.67	1.00	85	19.84	1.03	0.80	0.82	1.29
Cardiovascular diseases	65	5.82	1.32	0.06	0.99	1.76	31	7.27	1.41	0.09	0.95	2.09
Chronic respiratory diseases							9	2.13	1.56	0.27	0.70	3.47
Digestive diseases	10	0.93	1.25	0.51	0.63	2.48	10	2.45	1.62	0.20	0.77	3.39
Neurological disorders	70	6.25	1.49	0.005	1.13	1.96	23	5.27	1.47	0.06	0.98	2.22
DUBE[iii]	48	4.25	1.65	0.004	1.18	2.30	39	9.07	0.93	0.86	0.39	2.20
Other NCD	25	2.20	1.02	0.95	0.65	1.58	24	5.50	1.22	0.44	0.74	2.00
Injuries												
Transport injuries	247	21.93	0.73	<0.001	0.65	0.83	47	11.09	0.66	0.003	0.51	0.87
Unintentional injuries	95	8.48	0.94	0.59	0.75	1.17	28	6.61	1.13	0.60	0.72	1.75
Self harm	396	35.17	1.04	0.46	0.93	1.17	98	22.78	0.89	0.30	0.72	1.11
Interpersonal Violence	13	1.11	0.33	<0.001	0.19	0.56						

Causes contributing to less than 1% of total deaths are not shown. Causes where there were significant differences in mortality between the UK and EU15+ are highlighted in red.

[i] For EU15+ countries without data to 2015, I used lagged mean number of deaths over the three years prior to the latest available data year in poisson regression models for all countries except Greece, where data were only available for 2014. [ii] Mean annual number of deaths between 2013 and 2015 in the UK. [iii] Diabetes, urogenital, blood, endocrine disorders

Table 10: UK rank for three year lagged mean mortality rate per 100,000 compared with 16 EU15+ countries in 2015[i]

	Both sexes		Males	Females	Males	Females	Males	Females
	1 to 4	5 to 9	10 to 14	10 to 14	15 to 19	15 to 19	20 to 24	20 to 24
Communicable / maternal								
Common infections	17	17	16	16	17	17	16	17
Neonatal disorders	14	10						
Other communicable	14							
Non-communicable diseases								
Neoplasms	12	5	7	6	8	13	7	12
Cardiovascular diseases	15	14	12	12	15	12	12	16
Chronic respiratory diseases	15	17	17	17	15	17		14
Digestive diseases	16	17	16	15	15	17	13	14
Neurological disorders	12	7	13	12	16	16	15	15
DUBE[ii]	12	9	14	13	16	16	14	15
MSK[iii]						17		
Other non-communicable diseases	10	15	12	12	7	9	11	12
Injuries								
Transport injuries	5	5	11	8	7	8	6	6
Unintentional injuries	6	3	9	10	9	9	10	11
Self harm			5	6	10	5	8	7
Interpersonal violence	3	5	6	7	5	4	4	2

Causes contributing to less than 1% of total deaths are not shown. Cells are shaded according to UK mortality rank compared with 16 EU15+ countries from green (1 = lowest mortality) to yellow/orange (9 = median mortality) to red (17 = highest mortality) [i] Rank was calculated using three year lagged mean mortality rate per 100,000 for 2015 in the UK compared with all EU15+ countries except Greece. A rank of .5 means the UK had the same rank as another EU15+ country for that cause, sex and age group. For EU15+ countries without data to 2015, I used lagged mean mortality rate over the three years prior to the latest available data year. [ii]Diabetes, urogenital, blood, endocrine disorders; [iii]Musculoskeletal disorders.

Table 11: Change in UK rank for three year lagged mean mortality rate per 100,000 compared with 16 EU15+ countries between 2010 and 2015 [i]

	Both sexes		Males	Females	Males	Females	Males	Females
	1 to 4	5 to 9	10 to 14	10 to 14	15 to 19	15 to 19	20 to 24	20 to 24
Communicable / maternal								
Common infections	0	0	0	1	-2	-1	1	-6
Neonatal disorders	0	-4						
Other communicable	3							
Non-communicable diseases								
Neoplasms	-5	4	0	5	4	-2	-2	-4
Cardiovascular diseases	-4	3	-2	-3	0	2	1	-5
Chronic respiratory diseases	1	0	0	-1	-4	0		1
Digestive diseases	0	-1	-1	1	0	0	4	3
Neurological disorders	3	3	1	0	0	0	-1	-1
DUBE[ii]	1	5	-8	0	-1	0	0	0
MSK[iii]						-1		
Other NCD	0	-1	0	-1	5	4	2	1
Injuries								
Transport injuries	1	3	0	3	1	1	-1	1
Unintentional injuries	-2	1	-4	-1	-2	-2	-5	-1
Self Harm			-4	0	-5	0	0	1
Interpersonal violence	2	4	-3	0	1	1	0	1

Causes contributing to less than 1% of total deaths are not shown. Cells shaded green to indicate an improvement of more than two ranking paces since 2010 and red to indicate a worsening of two or more ranking places since 2010 [i] Change in rank was calculated using three year lagged mean mortality rate per 100,000 in the UK compared with all EU15+ countries except Greece in 2010 and 2015. For EU15+ countries without data to 2015, I used lagged mean mortality rate over the three years prior to the latest available data year. [ii]Diabetes, urogenital, blood, endocrine disorders; [iii]Musculoskeletal disorders.

Forecast trends in UK child and young person all-cause mortality compared with the EU15+ 2016 – 2040

Figures 27-31(p.120-124) show all-cause mortality rates in the UK and all 17 EU15+ countries are predicted to decline in all age groups the period between 2016-2040. However, comparisons between the UK and the EU15+ reveal some differential slopes in some age groups. Between 2016 and 2040, UK mortality in 1 to 4 is predicted to fall by 37.3% in males and 34.4% in females, whereas the EU15+ median is predicted to fall by 42.1% and 42.0% in males and females respectively. As a result, the difference in UK mortality rates compared with the EU15+ median is predicted to increase from 6.4% higher in 2016 to 15.4% higher by 2040 in males, and from 12.1% higher in 2016 to 26.6% higher by 2040 in females.

Reductions in UK mortality rates in 5 to 9 are predicted to exceed those of the EU15+ median slightly. UK mortality rates in 5 to 9 are predicted to fall by 41% in males, compared with 38.6% in the EU15+ median, and 33.5% in females, compared with 30.7% in the EU15+ median. As a result, UK estimates in 2040 are expected to be similar to the EU15+ median, eroding slight excess mortality in 2016. Reduction among 10 to 14 are between 2016 and 2040 are predicted to be similar to the EU15+ median, with the UK point estimate continuing to be comparable with the EU15+ median in both sexes. Amongst 10 to 14 UK mortality rates are predicted to fall by 32.9% in males, compared with 32.1% in the EU15+ median, and 26.6% in females, compared with 24.9% in the EU15+ median.

UK all-cause mortality in 15-19 in 2016 was comparable with the EU15+ median in both sexes, but reductions in mortality between 2016 and 2040 are predicted to be slower in the UK. By 2040, UK mortality rates in this age group are predicted to fall by 21.9% in males, compared with a 30.0% reduction in the EU15+ median, and 18.9% in females, compared with 27.9% in the EU15+ median. As a result, by 2040 UK mortality is predicted to be around 13% higher in males and 11.5% higher in females than the EU15+.

Amongst 20 to 24, the UK mortality rate estimate in 2016 was 12.2% lower than the EU15+ median in males, and comparable with the EU15+ median in females. However, similar to younger age groups, mortality declines are predicted to further lag behind the EU15+, such

that by 2040 mortality in 20 to 24 is predicted to be 3.1% higher than the EU15+ median in males and 8.9% higher in females.

Figure 27: Observed and predicted mortality rate per 100,000 in the UK compared with the EU15+ median, 90th and 10th centile from 2010 to 2040 in 1 to 4 year olds.

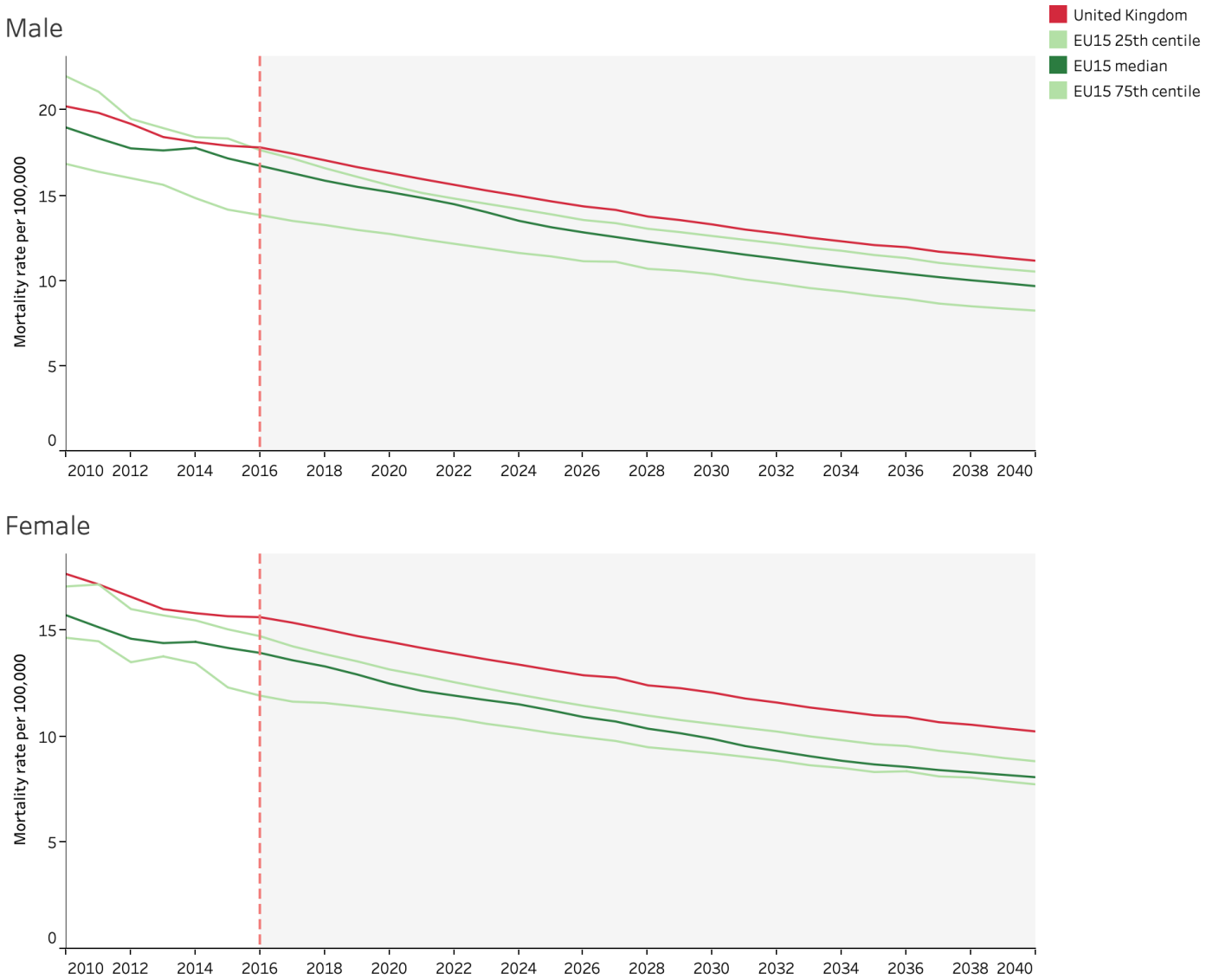


Figure 28: Observed and predicted mortality rate per 100,000 in the UK compared with the EU15+ median, 90th and 10th centile from 2010 to 2040 in 5 to 9 year olds.

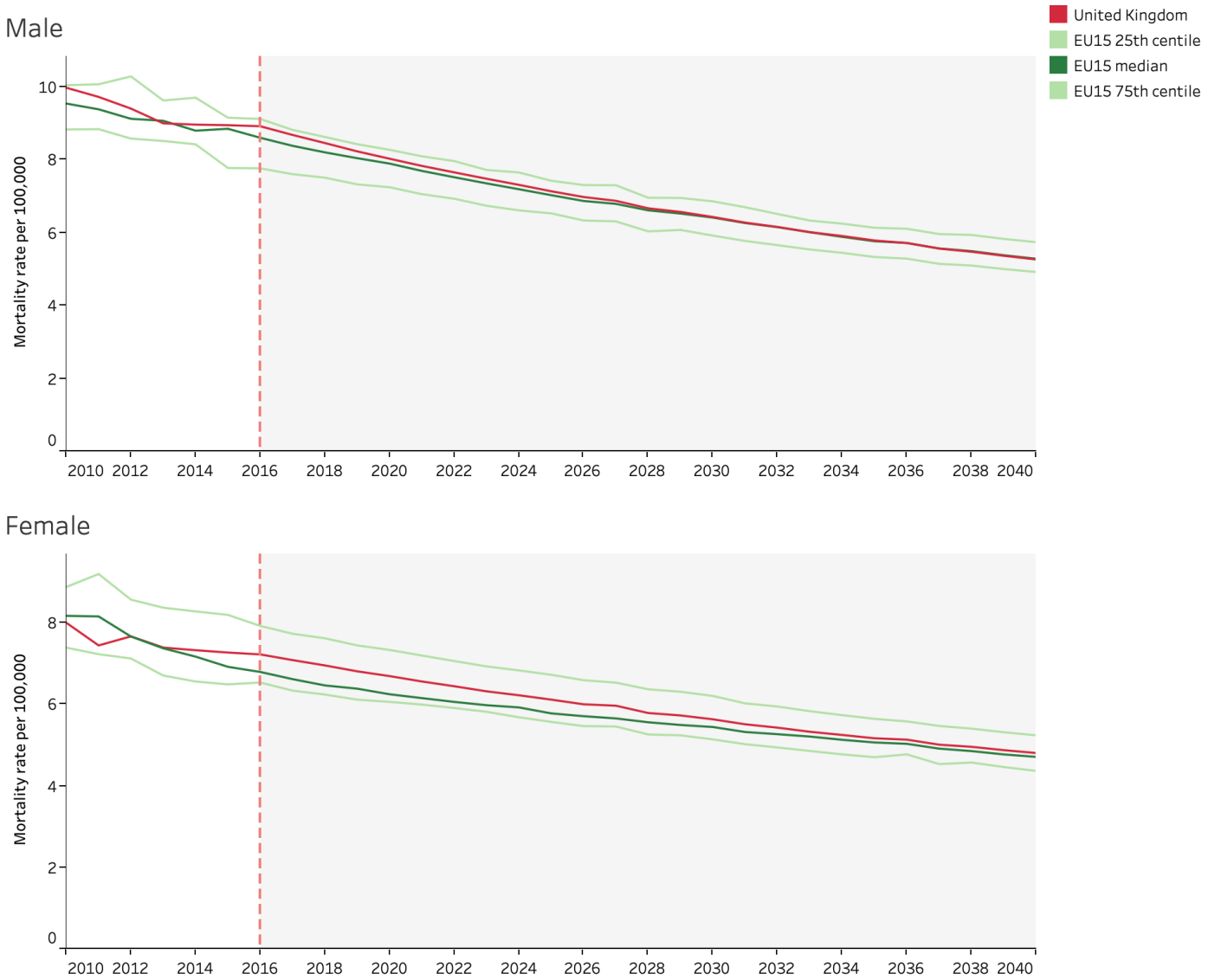


Figure 29: Observed and predicted mortality rate per 100,000 in the UK compared with the EU15+ median, 90th and 10th centile from 2010 to 2040 in 10 to 14 year olds.

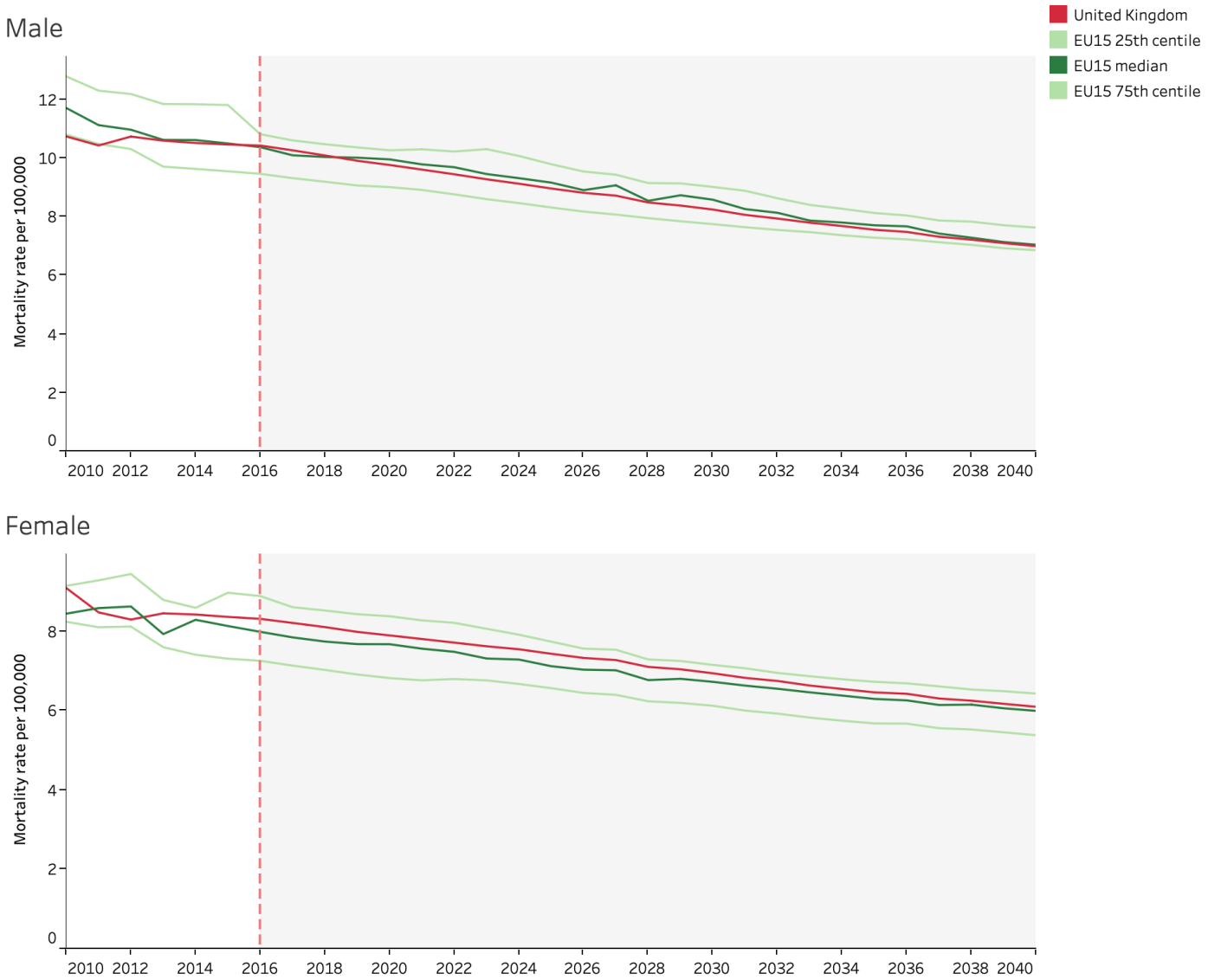


Figure 30: Observed and predicted mortality rate per 100,000 in the UK compared with the EU15+ median, 90th and 10th centile from 2010 to 2040 in 15 to 19 year olds.

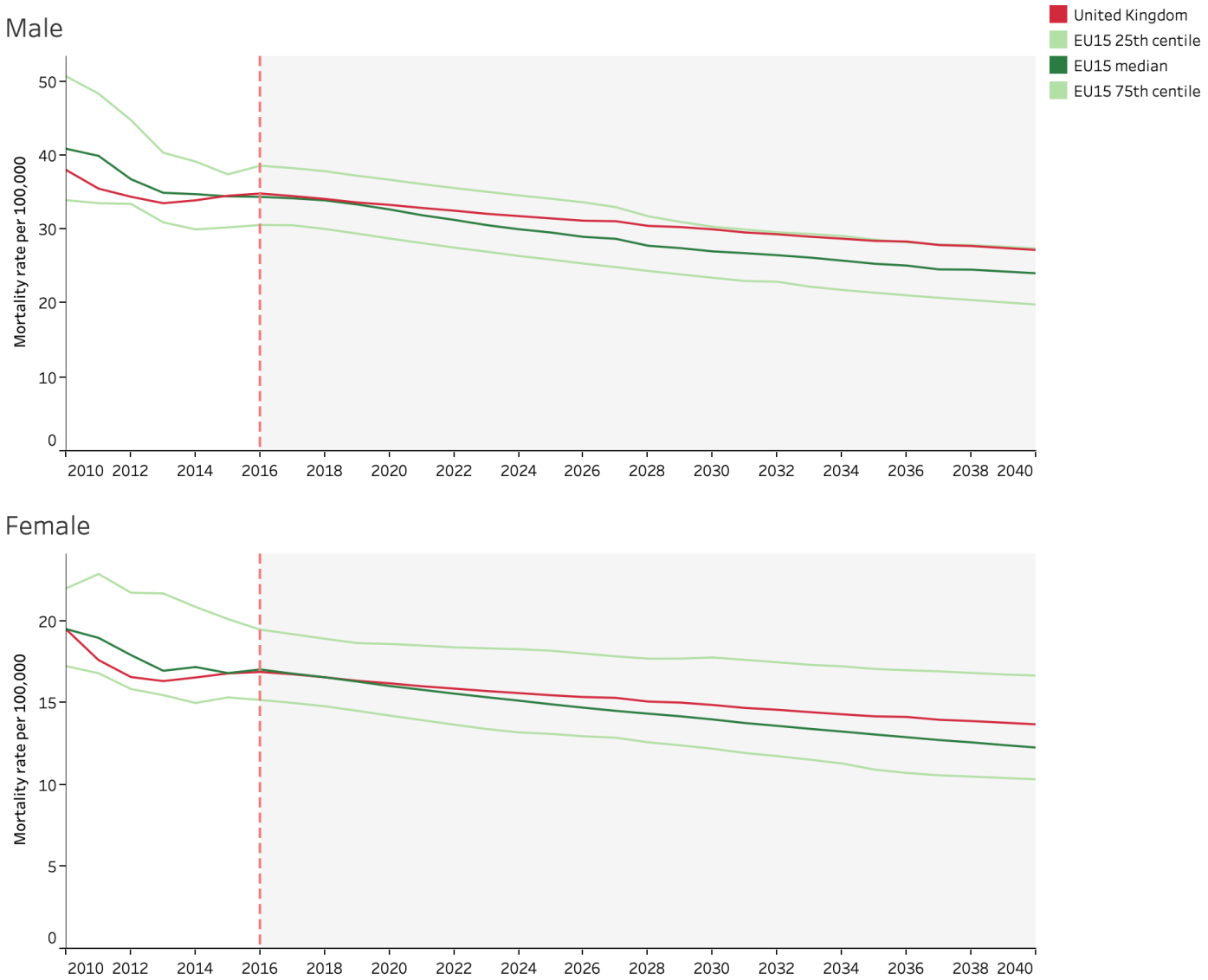
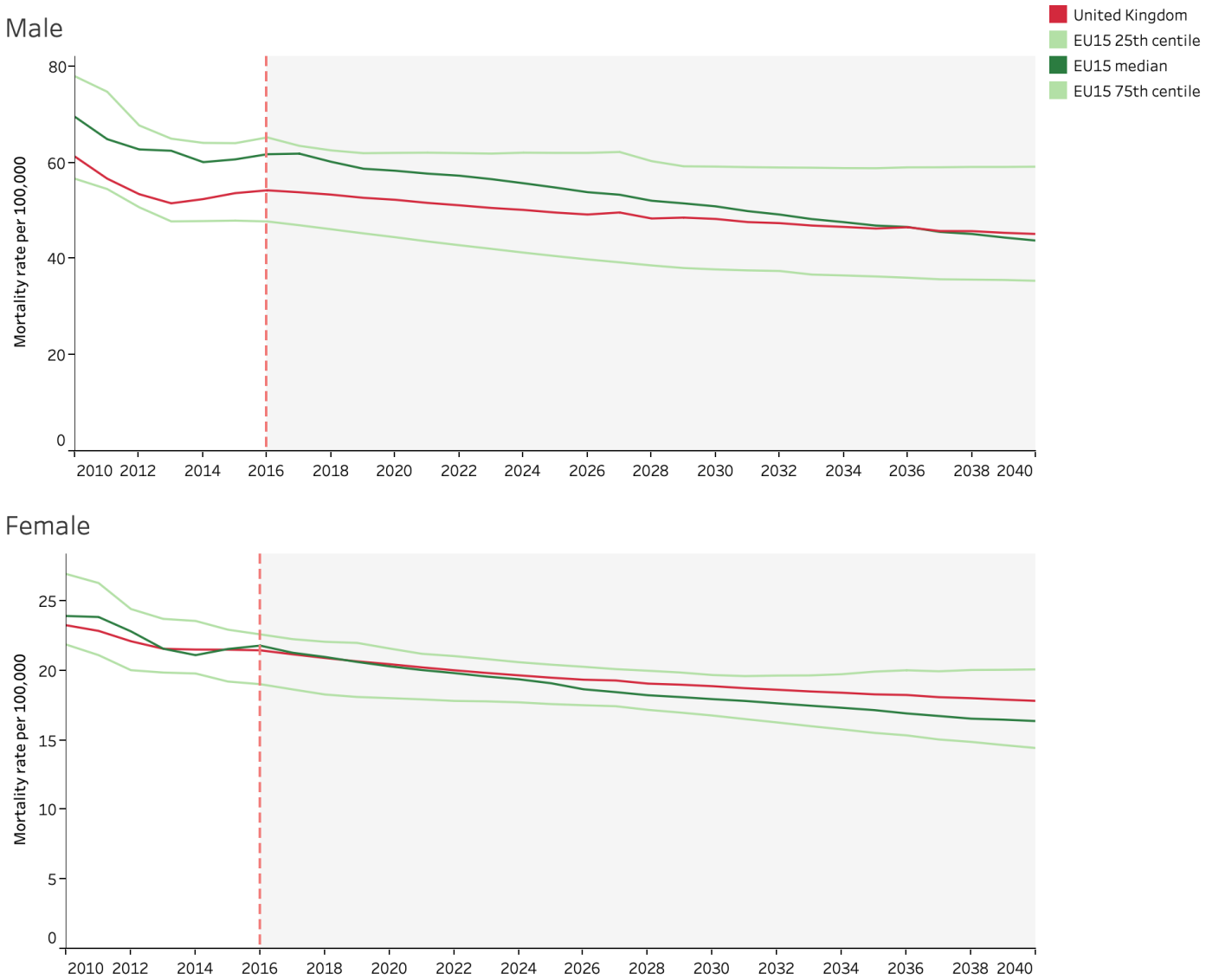


Figure 31: Observed and predicted mortality rate per 100,000 in the UK compared with the EU15+ median, 90th and 10th centile from 2010 to 2040 in 20 to 24 year olds.



Chapter 4 discussion

Slower rates of change in CYP mortality rates in the UK compared with the EU15+ between 1970 and 2016 have resulted in excess current UK mortality in all age groups 1-24. This is most pronounced in 1-4 year olds, where current outcomes have been consistently higher than the EU15+ median from the early 2000s, but trends are similar among adolescents and young adults. Current excess CYP mortality in the UK are driven by the specific cause groups where outcomes are poor. I found current UK CYP mortality to be significantly higher than the EU15+ for chronic respiratory conditions, neurological diseases, DUBE and common infections. The UK also ranked between highest or third highest for mortality from common infections across both sexes and all age groups, and ranked poorly for most NCD causes, particularly amongst adolescents. Although UK injury mortality appeared to be lower than the EU15+, there is evidence the UK's rank for some injury causes has worsened since 2010. More concerningly, forecast data suggest that disparities in all-cause mortality will increase, with the UK falling further behind the EU15+ for CYP mortality between 2016 – 2040 amongst young children 1-4 and adolescents 15-24.

Previous studies have shown a significant proportion of excess UK mortality to result from poor outcomes in younger children.[13,19,107] My findings build on this evidence, but further demonstrate stark differences in outcomes for older children and adolescents and young adults.[18] I found UK mortality for females 15-19 to be significantly higher than EU15+ countries for conditions accounting for around a quarter of total deaths in this age group. Adolescent females in the UK also ranked 16th or 17th in 5 out of the 10 NCD groups, and in the bottom half of countries for most other NCD causes. Amongst males 20-24, mortality rates were significantly higher for cause groups accounting for around 11% of all deaths.

These results are consistent with previous studies showing NCD causes to be a major contributor to higher than expected CYP mortality in the UK.[17,18,106,107] Similar to our findings, Viner et al. found the UK to have higher CYP mortality than the EU15+ for endocrine, respiratory, digestive, and particularly neuropsychiatric causes (epilepsy, cerebral palsy and substance misuse).[17] In our analysis, UK mortality for neurological causes (predominantly epilepsy) was significantly higher amongst adolescent girls (15-19) and young men (20-24).

The UK also ranked 15th or 16th out of 17 countries for neurological conditions amongst 15-24 year olds in both sexes. UK outcomes from chronic respiratory conditions, of which the majority were deaths due to asthma, were significantly worse amongst males and females 10-14. UK mortality for asthma in CYP has previously been shown to be up to 11 times higher than comparable countries,[106] and these differences appear to persist after adjustment for variation in prevalence.[108] Although we also found mortality for digestive conditions to be higher in the UK than the EU15+ in females aged 15-19, and for deaths due to DUBE within females 15-19 and males 20-24, this cause-groups contain a wide range of level 3 causes, and so these results are difficult to interpret.

These findings also highlight the contribution of communicable diseases to excess mortality amongst CYP, consistent with studies showing poor UK outcomes and slow rates of decline for childhood infections such as pneumonia and meningococcal disease.[107,108,137,203] The UK had significantly higher mortality for common infections than the EU15+ in 1-9 year olds (both sexes), males 10-14 and females 15-19, and ranked in the bottom three countries, across all age groups and both sexes for these causes.

The UK has historically performed well for injury mortality compared with other wealthy nations.[17] My findings support this, with significantly lower mortality for transport injuries amongst males 15-24 and females 20-24. However, there is evidence that the UK's position may be eroding. The UK dropped rank compared with the EU15+ between 2010 and 2015 for unintentional injuries, interpersonal violence and self-harm in male adolescents and young adults. Further, UK mortality rates for self-harm / interpersonal violence have actually increased since 2010 amongst adolescents (15-19), particularly males, whereas EU15+ median mortality for these causes has continued to decline.

Strengths and weaknesses

Where possible I used WHO World Mortality estimates for these analyses which have a high degree of data completeness and accuracy for countries included here. To improve comparability between countries and over time, I only included deaths coded to ICD 10, and used mean number of deaths and mortality rates over a three-year period to account for large

annual variability in mortality for some causes. All countries had data available within 1 year of the latest UK data release (2015), except Canada where data were available to 2013.

For cause specific analyses I used broad GBD level 2 cause-groups to reduce the risk of coding differences between countries and over time, but this approach has limitations due to the large number of conditions included in some groups. I considered mortality rates to be significantly different if $p<0.005$ to account for multiple testing within cause/age/sex groups. I defined this threshold a priori as using a Bonferroni correction across all 22 causes, age groups and both sexes would have been too conservative. However, these results may have differed using alternative approaches to account for multiple testing. Using this threshold for significant differences also risks underestimating UK excess mortality, particularly in adolescent males. The IRR for number of deaths from common infections, liver, neurological conditions and DUBE were all higher in the UK than EU15+ amongst males 15-19, with $p <0.05$ but >0.005.

As highlighted in Chapter 2, although the UK has high quality death registration systems, there are multiple shortcomings to death coding and delay in registration in the UK which affect estimates of the current burden of CYP mortality. Concerns around quality and reliability of death registration in countries within the EU15+, with many countries having systems which lack recent data and perform poorly compared with the UK, should also be considered when interpreting these results. Differences in the way countries compile mortality statistics, and whether deaths are reported by registration year or death year, may impact the international differences in outcomes shown here, particularly for recent data years.[204] Errors in death certification are common and vary by country and cause of death, complicating international mortality comparisons. Deaths due to self-harm are known to be under-reported,[135] and mortality due to common infections may be over-reported, with a large proportion actually attributable to underlying medical conditions.[13,136,137] However, as our results show excess UK mortality across a range of conditions in all age groups, they are unlikely to be fully explained by differences in coding alone.

I used forecast data provided by the Institute of Health Metrics and Evaluation for mortality in 1-24 in the UK and EU15+ countries from 2016 - 2040. These are high quality data, with the

authors reporting good out-of-sample fit when modelling mortality for 2007 – 2016 to fit data from 1990 – 2006.[201] However, caution must be used when interpreting any forecasting data. Forecast models used in GBD are in their infancy, and are likely to improve over time. Data shown here also are subject to limitations in the GBD estimation process, and many factors which will impact future health will be missed. Further years of observed data since 2016 are now available, with the release of GBD 2019 in the autumn of 2020, however the most recent forecast estimates are still from 2016. Analysing differences between observed to predicted data in these models, as more data-years become available, will be crucial to understanding their value moving forward.

Forecast estimates are also clearly vulnerable to large shifts in the drivers of health change or mortality shocks, such as the COVID-19 pandemic. Although the direct effects of the pandemic on CYP mortality in the UK and EU15+ countries are likely to be small, there have been substantial social, environmental and health service changes which may have brought benefits or harms to CYP, and are not captured in these data. The health impacts of economic disruption to CYP are also likely to be large, and vary between countries included in this analysis. However, these data do allow us to better understand possible future trends in CYP based on knowledge prior to the pandemic, describing how CYP deaths in the UK may continue to drift away from the EU15+ median in many age/sex groups, and so aid planning interventions to improve outcomes in the post COVID-19 world.

Here I limit forecasted analyses to all-cause mortality, however cause-specific predictions are also available, and may provide further insights. These may be particularly valuable with regard to mortality predictions for conditions I have identified where the UK currently performs poorly compared with the EU15+, and should be the focus of future study.

Conclusions

Slower rates of change in CYP mortality rates in the UK compared with the EU15+ between 1970 and 2016 have resulted in excess UK mortality amongst 1-24. This is most pronounced in 1-4 year olds, where outcomes have been consistently worse than the EU15+ median from the early 2000s, but trends are similar among adolescents and young adults.

Previous work has identified excess UK CYP mortality to be concentrated in young children. However, as all-cause comparisons are offset by good outcomes for injury, these conceal high mortality for deaths due to infections and non-communicable disease. This is particularly relevant for adolescents, where injury causes contribute to most of the mortality burden. When disaggregated by cause group, the UK has significantly higher mortality than the EU15+ for chronic respiratory conditions, neurological conditions, DUBE, digestive conditions and common infections. These differences affect all age groups and both sexes, and contribute to understanding current and projected excess CYP mortality in the UK.

Forecast data suggests the UK may continue to fall further behind the EU15+ for all-cause mortality in 1-4 and 15-24 year olds. Although these models do not capture the impact of the COVID pandemic on CYP mortality reductions, they do further highlight consequences of failing to address current concern around CYP deaths in the UK

Interpreting these findings, and understanding the mechanisms driving poor performance in UK CYP mortality, requires an understanding of variation in outcomes within the UK, which I will now explore in Chapter 5.

Chapter 5

Geographic variation in UK child and young person mortality

Background

In Chapter 4 I described how UK CYP mortality has declined at a slower rate than the EU15+, and that previous superiority in outcomes has been eroded. Forecast data suggest these differences are set to widen for younger children, and that although current UK mortality for adolescents and young adults is low compared with the EU15+, this is unlikely to remain the case by 2040. The analysis of current cause specific differences suggests high mortality in the UK for neurological conditions, respiratory conditions, common infections and diabetes/ endocrine conditions may explain some of these differences. However there are multiple other factors to consider, including exploring geographic variation in mortality outcomes within the UK.

As much of health and social policy in the UK is devolved, exploring mortality burden in Scotland, Northern Ireland, Wales and England separately is vital to understanding the UK's poor outcomes overall. Previous work has described wide geographic variation between and within UK countries for both adults[195,205,206] and CYP mortality,[44,62] however this work has focused mainly on all-cause differences. Patterns within the countries of the UK may also provide further insights, particularly in England, where 85% of the UK CYP population live.[207]

Regional differences within England may reflect compositional differences in populations, including ethnicity, age structure and deprivation. However, these may also represent different policy choices at national and local level, and the effectiveness of public health programmes. The Health and Social Care Act 2012 transferred responsibilities to provide several public health services in England from the NHS to local government from 2013,[208] with further child public health functions transferring in 2015.[209] This affected multiple public health functions which are associated with CYP mortality and morbidity. These include: services related to perinatal care and health visiting, NHS Child Measurement Programme, obesity and physical activity programmes, child (5-19) public health programmes, and those

relating to adolescents and young adults such as sexual health, substance misuse services, and targeted support for young mothers.[208] The breadth of public health functions now under local authority control highlights the need to understand variation in CYP mortality at this geographic level.

Here I describe variation in CYP mortality between the UK nations, 9 English regions and 150 English upper tier local authorities, by sex, 5-year age group, and cause of death in 1-24. I then compare subnational UK outcomes in all-cause mortality with the EU15+, to identify areas of the country which may be contributing most to the UK's poor performance internationally.

I would like to acknowledge the contribution of Prof. Bianca de Stavola, Professor of Medical Statistics, UCL GOS Institute of Child Health in formulating the methods used here to calculate confidence intervals around the EU15+ median mortality estimates.

Chapter 5 methods

Data

I requested subnational UK mortality data from the Institute of Health Metrics and Evaluation (IHME) through the GBD Collaborator Network. Estimates were available for the constituent countries of the UK (England, Wales, Scotland and Northern Ireland), the 9 Regions of England (London, South East, South West, West Midlands, East of England, East Midlands, Yorkshire and Humber, North East, North West), and within 150 upper tier local authorities in England.[205] Estimates were requested for 2017 for each location for number of deaths and mortality rates per 100,000 population for 1-4, 5-9, 10-14, 15-19, 20-24, by sex and cause of death (at level 1, 2 and 3 of the GBD cause hierarchy). These data are based on death registration, but are then modelled using the standard GBD estimation process as described in Chapter 2, with further details provided by Steel et al[205] and in GBD capstone publications.[120]

Subnational geographic areas within the UK

The 9 Regions of the England (formally Government Office Regions) are defined as level 1 Nomenclature of Territorial Units for Statistics (NUTS) areas within the European Union.[210] Although NUTS areas within England continue to be used to summarise regional statistics, they do not have administrative or policy responsibilities. Upper tier local authorities (hereafter referred to as "local authorities") comprise of 27 shire counties, 32 London boroughs, 1 City corporation (the City of London), 56 unitary authorities and 36 metropolitan districts.[211] City of London and Isles of Scilly were excluded from the GBD estimation process due to low population numbers, leaving estimates for 150 local authorities.

Analyses

I first describe range in mortality rate in 2017 between locations for all causes and the top ten causes of death at level 3 of the GBD hierarchy (described in supplementary material 2) within each age group and sex. I then calculated the ratio of the best to worst performing country, English Region or local authority, and then repeated this using the 90th and 10th centile within local authorities to account for extreme values. I did this to demonstrate inequality in outcomes between different parts of the UK, where a higher ratio represents greater variation in CYP mortality. I then used England as the baseline country to compare estimates, and considered mortality rates within each UK country, region, and local authority to be significantly different from England if upper and lower uncertainty bounds did not over-lap. This allowed me to create visualisations of differences between England and other parts of the country, and highlight where they occur. I also created geographic visualisations of UK CYP mortality in 2017 to describe this using Tableau mapping software, with spatial file data provided at www.tableaumapping.bi:443/wdc/.

Finally, I compared subnational UK estimates with the EU15+. To maintain consistency across locations, I compared these UK estimates with national level estimates for the 17 EU15+ countries provided by the GBD, rather than the World Mortality Database estimates used in Chapters 3 and 4. Although these will be similar, there are small differences due to the modelling involved in the GBD estimation process.[191,205] Similar to the analyses described above, I planned to use uncertainty intervals around subnational UK mortality estimates to identify and visualise differences from the EU15+. However, the GBD do not provide upper

and lower uncertainty intervals for the EU15+ as a whole, only for each country. In place of this, I used the median (i.e. 9th) value within the EU15+, and calculated 95% confidence intervals around this for each age/sex/cause group. I did this by first calculating the standard error for the mortality rate within each EU15+ country, age, sex and cause group using the maximum difference between the point estimate and the upper or lower uncertainty bounds provided by GBD divided by 1.96, (as the uncertainty bounds were not symmetrical). I then used the *rnormal* command in *Stata16* to sample a median value for each country, age, sex and cause group, from a normal distribution dictated by the point estimate and standard error. I did this to incorporate variation in the size of uncertainty intervals around estimates in different EU15+ countries, as a result of differences in population size (and other factors). I then calculated the median of these sampled values across the 17 EU15+ countries, and used bootstrap resampling with 1000 replications to estimate the standard error around this median. I finally calculated upper and lower confidence intervals using the observed EU15+ median value +/- the bootstrapped standard error multiplied by 1.96. Subnational UK mortality estimates were considered to differ from the EU15+ if upper and lower uncertainty bounds did not overlap with these 95% confidence intervals around the EU15+ median.

Chapter 5 results

Geographic variation between England, Scotland, Northern Ireland and Wales in 2017

Table 12 (p.134) summarises all-cause mortality rate per 100,000 with uncertainty bounds in 2017 in the UK and each UK country by age group and sex in 1-24. Tables 13-17 (p.137-141) show this for the top ten causes of death within each age group and sex. Cells are shaded red if the mortality rate is higher than England and uncertainty bounds around the estimates do not overlap, and green if the mortality rate is lower than England for that cause/sex/age group.

Table 12: All-cause mortality rate per 100,000 in 2017 for 1 to 24 year olds by sex in the United Kingdom and constituent countries

		England	Wales	Scotland	Northern Ireland	United Kingdom
1 to 4	Male	17.05 [16.73-17.38]	14.91 [10.59-20.01]	18.05 [13.01-24.16]	18.59 [14.13-23.89]	17.07 [16.51-17.62]
	Female	15.69 [15.39-15.97]	12.75 [8.97-17.56]	14.47 [11.38-18.31]	11.79 [9.75-14.37]	15.35 [14.95-15.76]
5 to 9	Male	7.60 [7.51-7.69]	9.83 [8.81-11.03]	12.36 [10.03-15.10]	6.11 [5.04-7.38]	8.00 [7.80-8.22]
	Female	5.82 [5.76-5.88]	6.48 [5.81-7.21]	6.33 [5.50-7.30]	9.03 [7.91-10.34]	5.99 [5.89-6.08]
10 to 14	Male	9.71 [9.64-9.79]	9.22 [8.56-9.99]	9.69 [8.55-10.99]	9.47 [8.35-10.66]	9.68 [9.56-9.82]
	Female	7.58 [7.53-7.64]	7.08 [6.60-7.64]	8.88 [8.11-9.74]	8.28 [7.57-9.06]	7.68 [7.60-7.76]
15 to 19	Male	27.97 [27.70-28.25]	37.27 [34.03-40.37]	42.68 [38.50-47.19]	46.09 [40.93-51.48]	30.17 [29.68-30.63]
	Female	15.62 [15.47-15.78]	18.86 [17.36-20.65]	20.02 [18.08-22.05]	15.87 [14.22-17.74]	16.14 [15.93-16.37]
20 to 24	Male	50.43 [49.93-50.97]	57.19 [52.22-61.98]	61.92 [55.76-68.28]	81.39 [72.42-90.79]	52.63 [51.86-53.38]
	Female	21.07 [20.85-21.29]	24.89 [22.75-27.48]	30.63 [27.34-33.96]	37.09 [32.99-41.90]	22.53 [22.17-22.91]

Mortality rate compared to England
Higher than England
Similar to England
Lower than England

Table 13 (p.137) shows mortality rates per 100,000 for 1-4 year olds within the UK and constituent countries for all-causes and the top ten causes of death. Using GBD estimates, in 2017 the all-cause mortality rate per 100,000 for 1-4 in the UK was 17.07 [16.51 – 17.62] amongst males and 15.35 [14.95 – 15.76] amongst females. Within the four countries of the UK, amongst males this ranged from 14.91 [10.59 – 20.01] in Wales to 18.59 [14-13 – 23.89] in Northern Ireland (1.2 fold difference), and amongst females this ranged from 11.79 [9.75 – 14.37] in Northern Ireland to 14.47 [11.38 – 18.31] in Scotland (1.3 fold difference).

The greatest difference in mortality between the best and worst performing country within the top 10 cases of death in 1-4 year olds was in lower respiratory tract infections in both sexes; there was a 1.5 fold difference in males (0.84 [0.54 – 1.27] in Wales vs. 1.27 [1.17-1.38] in England) and a 1.8 fold difference in females (0.7 [0.47 – 1.02] in Northern Ireland vs 1.27 [1.14 – 1.37] in England). Amongst males, mortality rates in UK countries were not significantly different from England for any cause. Amongst females, mortality rates were significantly lower than England for deaths from all-causes in Northern Ireland, and lower respiratory tract infections in Northern Ireland and Wales.

Amongst 5 to 9, the all-cause mortality rate per 100,000 in the UK was 8.00 [7.80 – 8.22] amongst males and 5.99 [5.89 – 6.08] amongst females (table 14, p.138). Amongst males this ranged from 6.11 [5.04 – 7.38] in Northern Ireland to 12.36 [10.03 – 15.10] in Scotland (2 fold difference). Amongst females this ranged from 5.82 [5.76 – 5.88] in England to 9.03 [7.91 – 10.34] in Northern Ireland (1.6 fold difference). The greatest range in outcomes by cause in this age group was in deaths due to road injuries in males (2.6 fold difference) and road injuries and other neurological disorders in females (1.9 fold difference). Amongst males, mortality rates were significantly higher in Scotland and Wales compared with England for all causes, road injuries and drowning. Mortality rates amongst males 5-9 in Northern Ireland were significantly lower than those in England for all-causes, lower respiratory tract infections, and other malignant neoplasms. Amongst females, mortality rates were higher in Northern Ireland compared with England for all-causes, road injuries, leukaemia, epilepsy, other neurological disorders and meningitis. Female all-cause and cause specific mortality rates in Scotland and Wales were similar to England in this age group.

Amongst 10 to 14 there was less variation in mortality between the nations of the UK than in other age groups (table 15, p.139). The all-cause mortality rate in the UK was 9.69 [8.56 – 9.82] in males and 7.68 [7.60 – 7.77] in females. Amongst males this ranged from 9.22 [8.56 – 9.99] in Wales to 9.71 [9.64 – 9.79] in England (1.05 fold difference) and in females this was 7.08 [6.60 – 7.64] in Wales to 8.88 [8.11 – 9.74] in Scotland (1.25 fold difference). In males the greatest range by cause was the mortality rate for other malignant neoplasms, which was around 1.6 fold higher in England than in Northern Ireland. Estimates were similar across the UK countries except all-cause mortality in females, which was significantly higher in Scotland compared with England.

Amongst 15 to 19, the all-cause mortality rate in the UK was 30.17 [29.68 – 30.63] in males and 16.14 [15.93 – 16.37] in females (table 16, p.140). Amongst males this ranged from 27.97 [27.7 – 28.25] in England to 46.09 [40.93 – 51.48] in Northern Ireland (1.6 fold difference), and amongst females this ranged from 15.62 [15.47 – 15.78] in England to 20.02 [18.08 – 22.05] in Scotland (1.28 fold difference). The all-cause mortality rate in England was significantly lower than all other UK nations and both sexes except females in Northern Ireland, where the mortality rate was similar to England. Amongst males, mortality rates were

higher than in England for: road injuries (Northern Ireland), drowning (Northern Ireland), self-harm (Northern Ireland and Scotland), leukaemia (Northern Ireland and Scotland), drug use disorders (Scotland and Wales) and other neurological disorders (Northern Ireland, Scotland and Wales). Amongst females, deaths due to drug use and asthma were significantly higher in Scotland and Wales than England.

Amongst 20-24, the all-cause mortality rate in the UK was 52.63 [51.86 – 53.38] in males and 22.53 [22.17 – 22.91] in females (table 17, p.141). Amongst males this ranged from 50.43 [49.93 – 50.97] in England to 81.39 [72.42 – 90.79] in Northern Ireland (1.6 fold difference). Amongst females this ranged from 21.07 [20.85 – 21.29] in England to 37.09 [32.99 – 41.90] in Northern Ireland (1.8 fold difference). All-cause mortality rates were significantly lower in England than in all other UK nations for both sexes. Amongst males, mortality rates were significantly higher than England for: self-harm (Northern Ireland and Scotland), road injuries (Northern Ireland), drug use disorder (Scotland), interpersonal violence (Northern Ireland and Scotland), leukaemia (Northern Ireland), other neurological disorders (Northern Ireland) and falls (Northern Ireland, Scotland and Wales). Amongst females, mortality rates were significantly higher than in England for: self-harm (Scotland and Northern Ireland), road injuries (Northern Ireland), drug use disorders (Northern Ireland and Scotland), epilepsy (Northern Ireland) and leukaemia (Northern Ireland and Scotland).

Table 13: Mortality rate per 100,000 in 2017 for 1 to 4 year olds in the UK and constituent countries for all causes and top ten causes of death in the UK by sex

		England	Wales	Scotland	Northern Ireland	United Kingdom
Male	All causes	17.05 [16.73-17.38]	14.91 [10.59-20.01]	18.05 [13.01-24.16]	18.59 [14.13-23.89]	17.07 [16.51-17.62]
	Congenital birth defects	3.16 [2.78-4.27]	2.83 [1.86-4.15]	3.28 [2.10-4.94]	3.51 [2.43-5.14]	3.16 [2.76-4.26]
	Lower respiratory infections	1.27 [1.17-1.38]	0.84 [0.54-1.27]	1.05 [0.66-1.60]	1.06 [0.70-1.57]	1.23 [1.13-1.34]
	Endocrine, metabolic, blood, and immune disorders	1.15 [0.78-1.30]	0.78 [0.45-1.34]	0.96 [0.57-1.54]	0.97 [0.61-1.54]	1.12 [0.78-1.29]
	Brain and nervous system cancer	0.94 [0.73-1.14]	0.79 [0.45-1.22]	0.97 [0.57-1.53]	0.98 [0.59-1.53]	0.94 [0.72-1.14]
	Meningitis	0.81 [0.71-0.94]	0.77 [0.46-1.18]	0.96 [0.60-1.46]	1.00 [0.61-1.57]	0.82 [0.71-0.94]
	Leukemia	0.79 [0.72-0.84]	0.74 [0.44-1.15]	0.87 [0.53-1.36]	0.91 [0.56-1.40]	0.80 [0.71-0.87]
	Other malignant neoplasms	0.77 [0.66-0.99]	0.65 [0.39-1.05]	0.81 [0.48-1.23]	0.69 [0.40-1.15]	0.76 [0.65-0.99]
	Road injuries	0.71 [0.65-0.75]	0.68 [0.41-1.06]	0.87 [0.53-1.35]	0.94 [0.58-1.43]	0.72 [0.66-0.78]
	Neonatal disorders	0.69 [0.61-0.76]	0.52 [0.31-0.81]	0.62 [0.37-0.99]	0.67 [0.40-1.04]	0.68 [0.60-0.75]

Mortality rate compared to England
- Higher than England
- Similar to England
- Lower than England

		England	Wales	Scotland	Northern Ireland	United Kingdom
Female	All causes	15.69 [15.39-15.97]	12.75 [8.97-17.56]	14.47 [11.38-18.31]	11.79 [9.75-14.37]	15.35 [14.95-15.76]
	Congenital birth defects	3.06 [2.65-4.18]	2.62 [1.66-3.98]	3.02 [2.06-4.31]	2.35 [1.65-3.43]	3.02 [2.59-4.09]
	Lower respiratory infections	1.27 [1.14-1.37]	0.76 [0.49-1.12]	0.85 [0.58-1.23]	0.70 [0.47-1.02]	1.20 [1.08-1.30]
	Endocrine, metabolic, blood, and immune disorders	1.05 [0.79-1.46]	0.75 [0.42-1.29]	0.87 [0.51-1.44]	0.72 [0.43-1.16]	1.02 [0.79-1.43]
	Other malignant neoplasms	0.84 [0.67-0.96]	0.69 [0.39-1.12]	0.79 [0.48-1.19]	0.54 [0.33-0.82]	0.82 [0.66-0.94]
	Leukemia	0.71 [0.62-0.77]	0.60 [0.34-1.00]	0.68 [0.43-1.06]	0.52 [0.33-0.80]	0.70 [0.61-0.77]
	Brain and nervous system cancer	0.69 [0.54-0.82]	0.58 [0.33-0.93]	0.67 [0.40-1.02]	0.51 [0.32-0.76]	0.67 [0.54-0.81]
	Meningitis	0.63 [0.55-0.75]	0.57 [0.33-0.87]	0.63 [0.41-0.91]	0.54 [0.35-0.81]	0.63 [0.54-0.74]
	Road injuries	0.60 [0.54-0.64]	0.49 [0.30-0.74]	0.55 [0.36-0.80]	0.51 [0.35-0.69]	0.59 [0.53-0.63]
	Other neurological disorders	0.52 [0.44-0.57]	0.51 [0.28-0.82]	0.56 [0.34-0.88]	0.46 [0.28-0.70]	0.52 [0.43-0.58]

Cells are shaded green if the mortality estimate is lower than England and red if the mortality rate estimate is higher than England, and uncertainty bounds do not overlap

Table 14: Mortality rate per 100,000 in 2017 for 5 to 9 year olds in the UK and constituent countries for all causes and top ten causes of death in the UK by sex

		England	Wales	Scotland	Northern Ireland	United Kingdom
Male	All causes	7.60 [7.51-7.69]	9.83 [8.81-11.03]	12.36 [10.03-15.10]	6.11 [5.04-7.38]	8.00 [7.80-8.22]
	Brain and nervous system cancer	0.99 [0.79-1.16]	1.17 [0.76-1.70]	1.48 [0.95-2.14]	0.73 [0.46-1.09]	1.03 [0.81-1.16]
	Congenital birth defects	0.84 [0.65-1.05]	0.97 [0.69-1.30]	1.21 [0.83-1.73]	0.58 [0.37-0.83]	0.86 [0.67-1.09]
	Road injuries	0.64 [0.60-0.68]	1.21 [0.85-1.60]	1.62 [1.06-2.28]	0.86 [0.56-1.37]	0.74 [0.68-0.81]
	Leukemia	0.69 [0.66-0.76]	0.93 [0.62-1.29]	1.14 [0.75-1.66]	0.59 [0.38-0.89]	0.73 [0.68-0.80]
	Other malignant neoplasms	0.50 [0.43-0.59]	0.52 [0.32-0.77]	0.62 [0.37-0.94]	0.27 [0.16-0.42]	0.50 [0.44-0.59]
	Endocrine, metabolic, blood, and immune disorders	0.48 [0.34-0.57]	0.50 [0.32-0.72]	0.59 [0.38-0.90]	0.30 [0.19-0.45]	0.48 [0.35-0.58]
	Lower respiratory infections	0.28 [0.27-0.30]	0.29 [0.19-0.42]	0.35 [0.23-0.53]	0.18 [0.11-0.26]	0.29 [0.27-0.31]
	Drowning	0.22 [0.20-0.23]	0.34 [0.24-0.48]	0.42 [0.28-0.60]	0.20 [0.13-0.30]	0.24 [0.22-0.25]
	Epilepsy	0.22 [0.19-0.23]	0.26 [0.18-0.37]	0.33 [0.22-0.49]	0.16 [0.10-0.24]	0.22 [0.19-0.24]

Mortality rate compared to England
- Higher than England
- Similar to England
- Lower than England

		England	Wales	Scotland	Northern Ireland	United Kingdom
Female	All causes	5.82 [5.76-5.88]	6.48 [5.81-7.21]	6.33 [5.50-7.30]	9.03 [7.91-10.34]	5.99 [5.89-6.08]
	Brain and nervous system cancer	0.70 [0.58-0.79]	0.80 [0.53-1.10]	0.75 [0.49-1.07]	1.04 [0.71-1.46]	0.72 [0.59-0.81]
	Congenital birth defects	0.63 [0.52-0.85]	0.72 [0.51-1.00]	0.71 [0.49-1.00]	1.03 [0.74-1.43]	0.65 [0.53-0.87]
	Road injuries	0.43 [0.40-0.46]	0.50 [0.35-0.67]	0.51 [0.35-0.70]	0.81 [0.56-1.11]	0.45 [0.42-0.49]
	Other malignant neoplasms	0.44 [0.36-0.48]	0.48 [0.31-0.70]	0.43 [0.29-0.63]	0.54 [0.35-0.78]	0.45 [0.37-0.49]
	Leukemia	0.41 [0.38-0.45]	0.53 [0.36-0.76]	0.54 [0.36-0.79]	0.74 [0.50-1.06]	0.44 [0.40-0.48]
	Endocrine, metabolic, blood, and immune disorders	0.41 [0.31-0.58]	0.45 [0.27-0.71]	0.43 [0.26-0.68]	0.58 [0.36-0.84]	0.42 [0.32-0.59]
	Lower respiratory infections	0.28 [0.26-0.30]	0.24 [0.16-0.34]	0.24 [0.16-0.34]	0.35 [0.25-0.51]	0.28 [0.26-0.30]
	Other neurological disorders	0.20 [0.18-0.22]	0.28 [0.18-0.42]	0.28 [0.18-0.41]	0.38 [0.23-0.56]	0.22 [0.19-0.24]
	Epilepsy	0.19 [0.18-0.20]	0.21 [0.14-0.30]	0.21 [0.14-0.30]	0.32 [0.21-0.46]	0.20 [0.18-0.21]

Cells are shaded green if the mortality estimate is lower than England and red if the mortality rate estimate is higher than England, and uncertainty bounds do not overlap

Table 15: Mortality rate per 100,000 in 2017 for 10 to 14 year olds in the UK and constituent countries for all causes and top ten causes of death in the UK by sex

		England	Wales	Scotland	Northern Ireland	United Kingdom
Male	All causes	9.71 [9.64-9.79]	9.22 [8.56-9.99]	9.69 [8.55-10.99]	9.47 [8.35-10.66]	9.68 [9.56-9.82]
	Road injuries	1.22 [1.14-1.28]	1.30 [0.98-1.67]	1.40 [1.01-1.84]	1.54 [1.13-2.13]	1.24 [1.17-1.32]
	Brain and nervous system cancer	0.84 [0.69-0.97]	0.74 [0.51-1.03]	0.75 [0.52-1.07]	0.76 [0.50-1.09]	0.82 [0.67-0.94]
	Congenital birth defects	0.73 [0.60-0.96]	0.67 [0.48-0.89]	0.74 [0.52-1.01]	0.68 [0.47-0.93]	0.73 [0.59-0.94]
	Leukemia	0.71 [0.68-0.77]	0.78 [0.52-1.09]	0.79 [0.52-1.11]	0.79 [0.53-1.13]	0.72 [0.68-0.79]
	Other malignant neoplasms	0.59 [0.50-0.67]	0.45 [0.29-0.65]	0.45 [0.28-0.64]	0.36 [0.23-0.54]	0.57 [0.50-0.65]
	Endocrine, metabolic, blood, and immune disorders	0.58 [0.45-0.73]	0.49 [0.33-0.69]	0.52 [0.35-0.74]	0.50 [0.32-0.74]	0.56 [0.44-0.71]
	Foreign body	0.51 [0.49-0.53]	0.50 [0.38-0.65]	0.51 [0.38-0.67]	0.50 [0.37-0.67]	0.51 [0.48-0.54]
	Other neurological disorders	0.35 [0.33-0.37]	0.54 [0.37-0.76]	0.54 [0.37-0.75]	0.51 [0.34-0.72]	0.38 [0.35-0.41]
	Epilepsy	0.35 [0.29-0.36]	0.29 [0.21-0.38]	0.31 [0.22-0.42]	0.30 [0.22-0.42]	0.34 [0.29-0.36]

Mortality rate compared to England
- Higher than England
- Similar to England
- Lower than England

		England	Wales	Scotland	Northern Ireland	United Kingdom
Female	All causes	7.58 [7.53-7.64]	7.08 [6.60-7.64]	8.88 [8.11-9.74]	8.28 [7.57-9.06]	7.68 [7.60-7.76]
	Road injuries	0.71 [0.67-0.75]	0.73 [0.53-0.97]	0.90 [0.67-1.19]	0.93 [0.68-1.23]	0.74 [0.69-0.78]
	Congenital birth defects	0.68 [0.56-0.94]	0.67 [0.48-0.89]	0.84 [0.61-1.14]	0.78 [0.54-1.08]	0.69 [0.56-0.95]
	Other malignant neoplasms	0.69 [0.55-0.74]	0.58 [0.39-0.83]	0.67 [0.44-0.95]	0.61 [0.39-0.86]	0.68 [0.55-0.74]
	Brain and nervous system cancer	0.67 [0.53-0.75]	0.61 [0.40-0.85]	0.77 [0.51-1.07]	0.70 [0.45-1.02]	0.67 [0.53-0.75]
	Endocrine, metabolic, blood, and immune disorders	0.57 [0.42-0.80]	0.47 [0.30-0.69]	0.61 [0.41-0.89]	0.59 [0.38-0.89]	0.57 [0.42-0.80]
	Leukemia	0.54 [0.51-0.59]	0.60 [0.39-0.84]	0.77 [0.53-1.06]	0.69 [0.47-0.98]	0.57 [0.53-0.62]
	Lower respiratory infections	0.28 [0.26-0.30]	0.22 [0.15-0.31]	0.28 [0.20-0.38]	0.25 [0.17-0.36]	0.28 [0.26-0.29]
	Asthma	0.26 [0.25-0.28]	0.28 [0.19-0.39]	0.35 [0.24-0.50]	0.34 [0.23-0.49]	0.27 [0.25-0.30]
	Epilepsy	0.26 [0.24-0.27]	0.24 [0.17-0.33]	0.30 [0.21-0.43]	0.28 [0.19-0.39]	0.26 [0.24-0.28]

Cells are shaded green if the mortality estimate is lower than England and red if the mortality rate estimate is higher than England, and uncertainty bounds do not overlap

Table 16: Mortality rate per 100,000 in 2017 for 15 to 19 year olds in the UK and constituent countries for all causes and top ten causes of death in the UK by sex

		England	Wales	Scotland	Northern Ireland	United Kingdom
Male	All causes	27.97 [27.70-28.25]	37.27 [34.03-40.37]	42.68 [38.50-47.19]	46.09 [40.93-51.48]	30.17 [29.68-30.63]
	Road injuries	7.08 [6.81-7.51]	8.84 [6.99-11.05]	8.70 [6.67-11.04]	11.96 [9.26-15.02]	7.45 [7.11-7.85]
	Self-harm	5.21 [5.02-5.40]	6.93 [5.33-8.58]	8.55 [6.64-10.45]	9.81 [7.65-12.38]	5.70 [5.43-5.99]
	Drug use disorders	1.89 [1.79-2.00]	3.46 [2.35-4.90]	5.57 [3.81-7.77]	2.23 [1.42-3.26]	2.27 [2.08-2.49]
	Other neurological disorders	1.11 [1.05-1.16]	1.86 [1.30-2.49]	1.95 [1.37-2.67]	2.15 [1.49-2.95]	1.25 [1.16-1.34]
	Other malignant neoplasms	1.04 [0.85-1.17]	1.02 [0.67-1.47]	1.18 [0.77-1.67]	1.07 [0.70-1.53]	1.05 [0.91-1.19]
	Leukemia	0.94 [0.89-0.98]	1.26 [0.87-1.76]	1.42 [1.01-1.98]	1.60 [1.10-2.35]	1.01 [0.95-1.08]
	Congenital birth defects	0.92 [0.71-1.23]	1.15 [0.80-1.59]	1.29 [0.93-1.79]	1.48 [1.00-2.04]	0.98 [0.76-1.28]
	Epilepsy	0.74 [0.62-0.77]	0.84 [0.60-1.14]	0.91 [0.65-1.25]	1.03 [0.72-1.42]	0.77 [0.66-0.81]
	Brain and nervous system cancer	0.68 [0.52-0.79]	0.83 [0.54-1.22]	0.85 [0.56-1.24]	1.04 [0.60-1.61]	0.71 [0.55-0.81]

Mortality rate compared to England
- Higher than England
- Similar to England
- Lower than England

		England	Wales	Scotland	Northern Ireland	United Kingdom
Female	All causes	15.62 [15.47-15.78]	18.86 [17.36-20.65]	20.02 [18.08-22.05]	15.87 [14.22-17.74]	16.14 [15.93-16.37]
	Road injuries	2.44 [2.32-2.56]	3.00 [2.27-3.82]	2.98 [2.21-3.90]	2.71 [2.02-3.49]	2.52 [2.40-2.66]
	Self-harm	1.98 [1.90-2.07]	1.91 [1.41-2.50]	2.34 [1.77-3.06]	1.70 [1.21-2.28]	2.00 [1.90-2.12]
	Drug use disorders	0.91 [0.86-0.96]	1.47 [1.00-2.06]	2.01 [1.40-2.76]	1.12 [0.76-1.59]	1.03 [0.96-1.12]
	Endocrine, metabolic, blood, and immune disorders	0.90 [0.62-1.18]	0.98 [0.63-1.50]	0.95 [0.59-1.41]	0.80 [0.51-1.20]	0.90 [0.62-1.18]
	Other malignant neoplasms	0.88 [0.73-1.00]	1.07 [0.72-1.55]	0.97 [0.67-1.40]	0.71 [0.44-1.02]	0.89 [0.74-1.00]
	Congenital birth defects	0.85 [0.65-1.14]	1.03 [0.71-1.39]	1.10 [0.78-1.48]	0.89 [0.62-1.23]	0.88 [0.67-1.16]
	Epilepsy	0.71 [0.67-0.75]	0.82 [0.59-1.12]	0.80 [0.56-1.09]	0.69 [0.49-0.96]	0.72 [0.67-0.77]
	Leukemia	0.64 [0.61-0.68]	0.88 [0.59-1.27]	0.88 [0.63-1.24]	0.73 [0.49-1.05]	0.68 [0.63-0.74]
	Brain and nervous system cancer	0.53 [0.42-0.60]	0.65 [0.39-0.94]	0.63 [0.40-0.92]	0.51 [0.32-0.74]	0.54 [0.42-0.60]

Cells are shaded green if the mortality estimate is lower than England and red if the mortality rate estimate is higher than England, and uncertainty bounds do not overlap

Table 17: Mortality rate per 100,000 in 2017 for 20 to 24 year olds in England compared with Northern Ireland, Scotland and Wales for all causes and top ten causes of death by sex*

		England	Wales	Scotland	Northern Ireland	United Kingdom
Male	All causes	50.43 [49.93-50.97]	57.19 [52.22-61.98]	61.92 [55.76-68.28]	81.39 [72.42-90.79]	52.63 [51.86-53.38]
	Self-harm	12.95 [12.48-13.37]	14.34 [11.53-17.21]	16.79 [13.77-20.28]	26.35 [21.29-31.67]	13.73 [13.18-14.25]
	Road injuries	10.53 [10.16-10.94]	10.13 [7.88-12.65]	8.90 [6.89-11.32]	14.99 [11.29-18.98]	10.51 [10.14-10.95]
	Drug use disorders	6.43 [6.13-6.75]	9.41 [6.53-12.69]	12.93 [9.38-17.15]	8.52 [5.70-12.16]	7.18 [6.73-7.72]
	Epilepsy	1.28 [1.12-1.35]	1.33 [0.96-1.76]	1.27 [0.95-1.67]	1.81 [1.31-2.42]	1.30 [1.17-1.38]
	Other malignant neoplasms	1.17 [0.98-1.25]	1.04 [0.70-1.48]	1.02 [0.68-1.43]	1.18 [0.77-1.71]	1.16 [0.98-1.25]
	Interpersonal violence	0.98 [0.93-1.02]	1.25 [0.85-1.80]	1.63 [1.12-2.29]	2.10 [1.44-2.93]	1.08 [1.01-1.15]
	Congenital birth defects	1.03 [0.75-1.34]	1.13 [0.77-1.52]	1.17 [0.82-1.61]	1.50 [1.05-2.05]	1.06 [0.78-1.37]
	Leukemia	0.98 [0.93-1.04]	1.17 [0.80-1.62]	1.05 [0.74-1.46]	1.50 [1.04-2.13]	1.01 [0.95-1.07]
	Other neurological disorders	0.94 [0.89-0.99]	1.33 [0.91-1.86]	1.27 [0.87-1.74]	1.64 [1.13-2.29]	1.01 [0.94-1.07]

		England	Wales	Scotland	Northern Ireland	United Kingdom
Female	All causes	21.07 [20.85-21.29]	24.89 [22.75-27.48]	30.63 [27.34-33.96]	37.09 [32.99-41.90]	22.53 [22.17-22.91]
	Self-harm	3.41 [3.29-3.54]	3.46 [2.72-4.41]	5.30 [4.25-6.54]	5.36 [4.05-6.85]	3.63 [3.48-3.81]
	Road injuries	2.27 [2.16-2.36]	2.62 [1.96-3.46]	2.92 [2.19-3.72]	4.22 [3.03-5.65]	2.40 [2.28-2.52]
	Drug use disorders	1.84 [1.76-1.94]	2.79 [1.91-3.78]	3.88 [2.78-5.20]	3.96 [2.80-5.43]	2.12 [1.98-2.28]
	Epilepsy	1.06 [1.01-1.11]	1.17 [0.87-1.57]	1.22 [0.89-1.60]	1.76 [1.25-2.41]	1.10 [1.03-1.17]
	Endocrine, metabolic, blood, and immune disorders	0.98 [0.62-1.19]	0.95 [0.61-1.38]	1.07 [0.63-1.55]	1.39 [0.87-2.01]	1.00 [0.63-1.21]
	Congenital birth defects	0.78 [0.62-1.07]	0.94 [0.68-1.26]	1.13 [0.78-1.59]	1.42 [0.99-1.97]	0.83 [0.65-1.14]
	Other malignant neoplasms	0.73 [0.65-0.82]	0.87 [0.59-1.23]	0.87 [0.58-1.24]	1.12 [0.73-1.60]	0.76 [0.68-0.85]
	Leukemia	0.66 [0.63-0.70]	0.88 [0.63-1.25]	1.04 [0.76-1.44]	1.26 [0.88-1.79]	0.72 [0.68-0.79]
	Brain and nervous system cancer	0.62 [0.50-0.67]	0.75 [0.50-1.07]	0.75 [0.51-1.05]	1.01 [0.64-1.44]	0.65 [0.51-0.71]

Mortality rate compared to England
- Higher than England
- Similar to England
- Lower than England

Cells are shaded green if the mortality estimate is lower than England and red if the mortality rate estimate is higher than England, and uncertainty bounds do not overlap.

Geographic variation within 9 English regions

Table 18 (p.143) shows the all-cause mortality rate per 100,000 with uncertainty bounds in 2017 in England and within the 9 English Regions, by age group and sex. Cells are shaded green if the mortality rate estimate is significantly lower than England, and red if this is significantly higher than England.

In the South East, mortality rates were significantly lower than England for all age groups and both sexes, as were estimates in the South West except for 15-19 females and 20-24 in both sexes. By contrast, mortality rates in the North West were significantly higher than England in all age/sex groups except males 5-9 and 20-24. In most age/sex groups, mortality rates were also significantly worse than England in Yorkshire and the Humber and West Midlands. The East of England, East Midlands and North East showed a mixed picture, as did London, where mortality rates were significantly higher than England in younger age groups and significantly lower than England in adolescents and young adults.

Table 18: All-cause mortality rate with uncertainty bounds in 2017 in England and the 9 English Regions by age group and sex

		England	North West England	North East England	Yorkshire and the Humber	West Midlands	East of England	East Midlands	Greater London	South West England	South East England
1 to 4	Male	17.05 [16.73-17.38]	19.94 [18.98-20.98]	16.92 [15.55-18.30]	18.47 [17.32-19.66]	21.14 [19.82-22.48]	15.60 [14.50-16.77]	16.17 [14.77-17.63]	16.85 [16.29-17.49]	15.52 [14.39-16.60]	13.63 [12.87-14.42]
	Female	15.69 [15.39-15.97]	18.83 [18.01-19.71]	15.96 [14.64-17.21]	16.98 [16.11-17.91]	16.54 [15.63-17.47]	13.37 [12.27-14.48]	14.45 [13.15-15.91]	17.85 [17.35-18.39]	12.63 [11.70-13.61]	13.05 [12.47-13.66]
5 to 9	Male	7.60 [7.51-7.69]	7.35 [7.12-7.60]	5.91 [5.71-6.11]	7.38 [7.10-7.66]	9.05 [8.74-9.37]	7.95 [7.63-8.28]	7.97 [7.61-8.38]	8.63 [8.48-8.78]	7.12 [6.82-7.41]	6.20 [6.00-6.40]
	Female	5.82 [5.76-5.88]	7.75 [7.55-7.95]	5.05 [4.90-5.20]	7.59 [7.34-7.84]	7.63 [7.42-7.83]	4.93 [4.74-5.13]	3.07 [2.94-3.20]	6.09 [6.01-6.18]	5.48 [5.29-5.66]	4.11 [3.99-4.23]
10 to 14	Male	9.71 [9.64-9.79]	13.45 [13.16-13.73]	10.64 [10.39-10.89]	8.86 [8.66-9.09]	12.43 [12.15-12.71]	8.82 [8.59-9.07]	9.60 [9.31-9.89]	7.90 [7.79-8.00]	9.26 [9.01-9.52]	7.87 [7.69-8.06]
	Female	7.58 [7.53-7.64]	8.35 [8.19-8.53]	7.13 [6.94-7.30]	10.82 [10.61-11.07]	7.48 [7.33-7.64]	5.19 [5.06-5.33]	7.73 [7.50-7.96]	8.99 [8.88-9.10]	6.95 [6.79-7.11]	5.73 [5.61-5.85]
15 to 19	Male	27.97 [27.70-28.25]	33.72 [32.87-34.55]	33.45 [32.38-34.55]	34.79 [33.83-35.77]	27.55 [26.74-28.40]	20.53 [19.82-21.30]	31.65 [30.55-32.72]	25.39 [24.94-25.86]	25.21 [24.45-25.99]	25.03 [24.33-25.78]
	Female	15.62 [15.47-15.78]	19.53 [19.04-20.00]	15.02 [14.55-15.51]	14.03 [13.66-14.40]	16.95 [16.46-17.45]	17.42 [16.84-18.03]	15.97 [15.40-16.56]	11.80 [11.57-12.03]	19.89 [19.34-20.39]	12.43 [12.09-12.76]
20 to 24	Male	50.43 [49.93-50.97]	48.44 [47.24-49.63]	61.00 [58.96-63.21]	58.34 [56.74-59.98]	46.92 [45.58-48.33]	55.67 [53.74-57.77]	60.27 [58.13-62.39]	39.87 [39.16-40.54]	51.32 [49.87-52.89]	48.03 [46.66-49.52]
	Female	21.07 [20.85-21.29]	23.18 [22.54-23.79]	16.10 [15.53-16.71]	24.47 [23.77-25.10]	29.39 [28.40-30.36]	23.39 [22.51-24.26]	16.28 [15.62-16.92]	16.65 [16.32-16.97]	25.54 [24.80-26.29]	16.34 [15.88-16.83]

Mortality rate compared to England

- Higher than England
- Similar to England
- Lower than England

Cells are shaded green if the mortality estimate is lower than England and red if the mortality rate estimate is higher than England, and uncertainty bounds do not overlap.

Geographic variation in child and young person mortality within English local authorities

Figures 32 and 33 (p.147-148) show all-cause mortality rate per 100,000 in 2017 within the 150 English local authorities by age group and sex. Tables within supplementary material 2 show estimates for mortality rates per 100,000 with uncertainty bounds for all 150 English local authorities for all causes and the top 10 causes of death within each age and sex group.

Broadly, mortality rates were higher in the North West and North East of England compared with London and the South East for all age groups, although there was considerable variation within this. Amongst males aged 1 to 4, the all-cause mortality rate per 100,000 ranged from 9.1 [7.36 – 11.18] in Surrey to 34.68 [24.62 – 47.93] in Blackburn and Darwen (3.8 fold difference) and the ratio between the 90th to 10th percentile local authority was 1.8. Within the top 10 causes of death in this age group, the greatest variation in mortality between local authorities was in road injuries and meningitis (both 4.9 fold difference), and the largest difference between the 90th and 10th percentile for mortality was in lower respiratory tract infections, meningitis and drowning (2.1 fold difference). Amongst females aged 1 to 4, variation in outcomes was greater than in males, with all-cause mortality ranging from 5.58 [3.94 – 7.89] in Rutland to 30.97 [21.91 – 42.36] in Knowsley (5.6 fold difference), but the ratio of the 90th to 10th percentile was similar to males (1.9). Within the top 10 causes of death in the UK in this age/sex group, neonatal disorders had the greatest variation in outcomes between the best and worst performing local authority (9.7 fold difference), with lower respiratory tract infections and meningitis having the greatest variation between the 90th and 10th percentile local authority (2.3 fold difference).

Amongst 5 to 9 males, all-cause mortality within local authorities ranged from 2.03 [1.84 – 2.25] in Newcastle upon Tyne to 18.23 [15.61 – 20.84] in Southend-on-Sea (9.0 fold difference), and the ratio of 90th to 10th percentile all-cause mortality was 2.7. Within the top 10 causes of death, the greatest variation in outcomes was in deaths due to epilepsy (13.2 fold difference), with the greatest difference in mortality between the 90th to 10th percentile seen in lower respiratory tract infections (3.6 fold difference). Amongst females, all-cause mortality ranged from 1.51 [1.26 – 1.79] in Rutland to 25.65 [24.09 – 27.29] in Hillingdon (17 fold difference), and the ratio of 90th to 10th percentile was 3.7. Within the top 10 causes of

death, lower respiratory tract infections had both the greatest range in estimates (27.7 fold difference), and greatest difference between the 90th and 10th percentile estimates (4.8 fold difference).

Amongst males aged 10-14 all-cause mortality ranged from 3.90 [3.63 – 4.19] in Kingston upon Thames to 23.44 [20.94 – 26.12] in Solihull (6 fold difference), with a 2.8 fold difference between the 90th and 10th percentile local authorities. Asthma showed the greatest range in outcomes within the top 10 causes of death (11 fold difference), and the greatest difference between the 90th and 10th percentile (4.2 fold difference). Amongst females 10-14, all-cause mortality ranged from 2.90 [2.61 – 3.21] on the Isle of Wight to 21.96 [20.53 – 23.54] in Oldham (7.6 fold difference), with a 3.0 fold difference between the 90th and 10th percentile local authorities. Similar to males, the greatest difference within the top 10 causes of death was in deaths due to asthma (19.8 fold difference), with a 3.7 fold difference between the 90th and 10th percentiles.

Amongst male adolescents aged 15-19, all-cause mortality ranged from 13.88 [12.48 – 15.43] in Hertfordshire to 58.24 [52.13 – 65.51] in Darlington (4.2 fold difference), and the ratio of mortality estimates in the 90th to 10th percentile local authorities was 2.1. Amongst females 15-19 this ranged from 1.84 [1.66 – 2.02] in Bexley to 31.44 [28.53 – 34.80] in Knowsley (17 fold difference), and the ratio of 90th to 10th percentiles was 2.2 (similar to males). Amongst males and females, the greatest difference in mortality amongst the top 10 causes of death was in drug use disorders, where there was a 10.4 fold difference in males and a 49.4 fold difference in females; the ratio of outcomes in the 90th to 10th percentiles was 3.6 in both sexes.

Amongst young adults 20-24, all-cause mortality in males ranged from 24.18 [21.97 – 26.46] in Manchester to 97.43 [87.41 – 108.13] in North Lincolnshire (4.0 fold difference) and the ratio of the 90th percentile to 10th percentile was 2.1. Amongst females 20-24 the range was 8.94 [8.08 – 9.83] in Manchester to 59.80 [53.62 – 66.26] in Rotherham (6.7 fold difference) and the ratio of the 90th percentile to 10th percentile was 2.3. Similar to 15-19 year olds, the greatest variation in outcomes was in mortality due to drug use, where there was a 7.6 fold difference in outcomes amongst males and an 11 fold difference in females. The difference

between the 90th and 10th percentile estimates was greatest in other neurological disorders in males (2.6 fold difference) and in drug use disorders in females (3.2 fold difference).

Figure 32: All-cause mortality per 100,000 within English Local Authorities amongst males in 2017

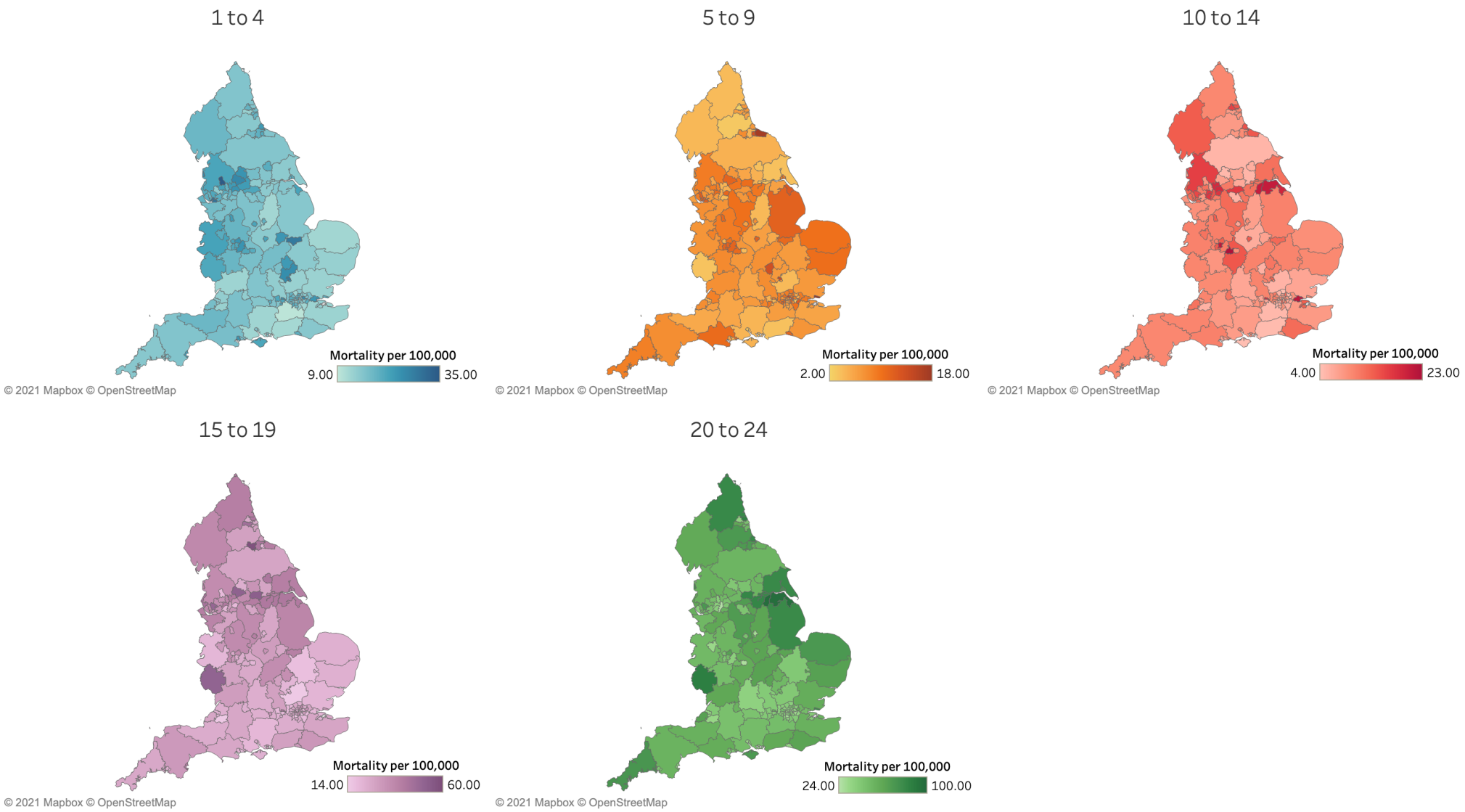
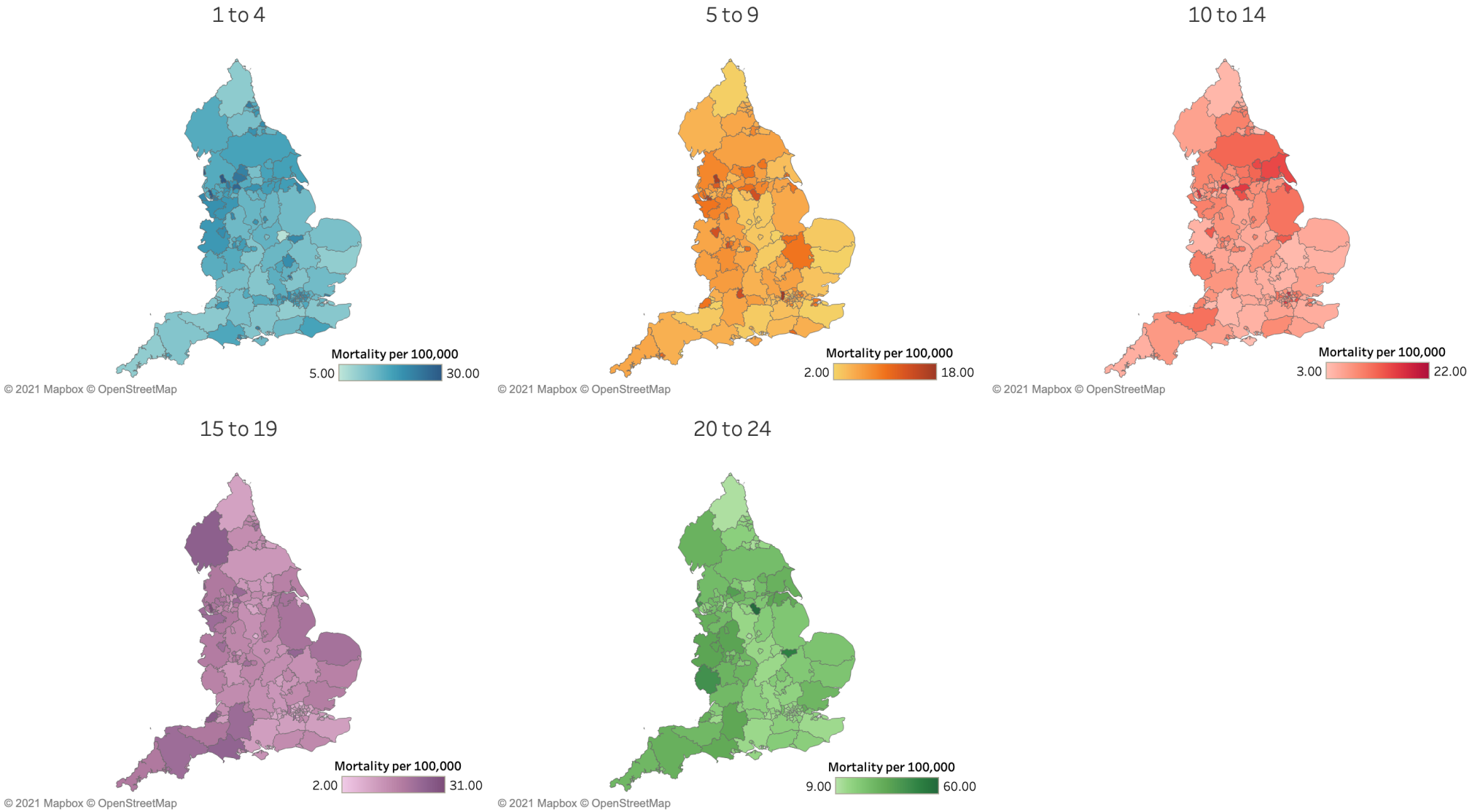


Figure 33: All-cause mortality per 100,000 within English Local Authorities amongst females in 2017



UK regional mortality compared with the EU15+

Figure 34 (p.152) shows all-cause mortality rate per 100,000 in 2017 for both sexes in 1 to 4, 5 to 9, 10 to 14, 15 to 19 and 20 to 24 in the UK, England, Scotland, Wales, Northern Ireland, the 9 English regions and 17 EU15+ countries. EU15+ median mortality is shown as a red bar, and the size of each mark is proportional to the location population size. The all-cause mortality rate per 100,000 with upper and lower uncertainty bounds for estimates in each UK country, English region and English local authority, compared with the EU15+ median is shown with associated maps in figures 35-49 (p.153-167). Local authorities are shaded green if the mortality rate is significantly lower than the EU15+ and red if this is significantly higher than the EU15+.

Amongst 1 to 4 year olds, the EU15+ median mortality rate per 100,000 in 2017 was 15.78 [13.32 - 18.24] amongst males and 11.73 [9.77 – 13.70] amongst females. Mortality rates for males in the UK and constituent countries were similar to the EU15+ median in this age group, and amongst English Regions estimates were higher than the EU15+ median in the Northwest of England and West Midlands. At the local authority level, amongst males 1-4 only Surrey had a mortality rate lower than the EU15+ median, and 26 local authorities (17.3%) had estimates which were higher than the EU15+ median. Amongst females 1-4, mortality rates were higher than the EU15+ median for the whole of the UK, England, and 5 out of 9 English regions. Only Rutland had a mortality rate lower than the EU15+ median, and 75 (50%) local authorities had estimates which were higher than the EU15+ median.

The EU15+ median mortality for children aged 5-9 in 2017 was 8.22 [7.38 – 9.08] amongst males and 6.80 [5.97 – 7.64] amongst females. Amongst males 5-9, mortality rates in the UK, England and Wales were similar to the similar to the EU15+ median, and they were lower in Northern Ireland and higher in Scotland. No English region had a mortality rate higher than the EU15+ median, and estimates were lower in the North East and South East. 32 (21.3%) local authorities had estimates higher than the EU15+ median and 48 (32.0%) local authorities had estimates which were lower than the EU15+ median. Amongst females 5-9, the overall UK estimate was similar to the EU15+ median, the estimate in Northern Ireland was higher, and the estimate in England lower. Mortality rates were lower than the EU15+ median in 5/9

English regions. 33 (22.0%) local authorities had estimates higher than the EU15+ median and 79 (52.7%) of local authorities had estimates which were lower than the EU15+ median.

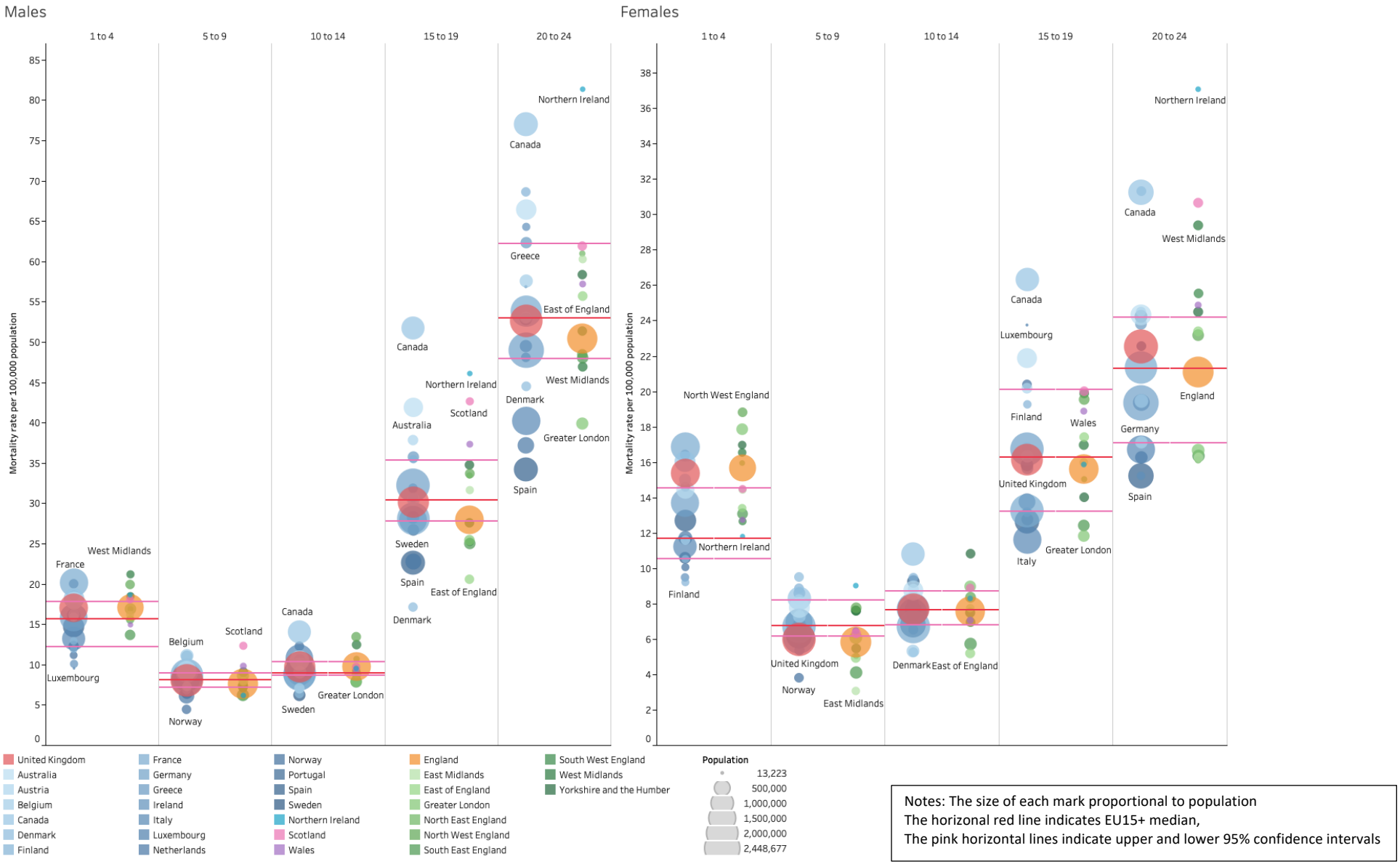
The EU15+ median mortality for young people aged 10-14 in 2017 was 9.09 [8.21 – 9.97] amongst males and 7.71 [6.99 – 8.43] amongst females. Estimates in the UK and constituent countries were similar to the EU15+ median for both sexes. Amongst males 10-14, within English regions the mortality rate was higher than the EU15+ median in the North East, North West and West Midlands, and lower than the EU15+ median in London and the South East. 52 (34.7%) local authorities had estimates which were higher than EU15+ median, and 41 (27.3%) had estimates which were lower than the EU15+ median. Amongst females 10-14, estimates were higher than the EU15+ median for London and Yorkshire and the Humber, and lower in the East of England and South East. 47 (31.3%) local authorities had estimates which were higher than the EU15+ median and 63 (42.0%) local authorities had estimates which were lower than the EU15+ median.

The EU15+ median mortality rate for 15-19 in 2017 was 30.47 [26.93 – 34.01] amongst males and 16.32 [13.44 – 19.19] amongst females. Amongst males 15-19, the mortality rate for the UK and England was similar to the EU15+ median, but higher in Scotland, Wales and Northern Ireland. Mortality rates were lower than the EU15+ median in 4/9 English regions. 30 (20.0%) local authorities had estimates higher than the EU15+ median for males 15-19, and 56 (37.3%) local authorities had estimates lower than the EU15+ median. Amongst females 15-19, estimates within the UK and all constituent countries were similar to the EU15+ median. The estimates in the South West England was higher than the EU15+ median, and estimates in London and the South East lower. 22 (14.7%) local authorities had estimates higher than the EU15+ median, and 37 (24.7%) had estimates lower than the EU15+ median.

Amongst 20-24, the EU15+ median mortality in 2017 was 53.07 [46.48 – 59.65] amongst males and 21.35 [17.93 – 24.77] amongst females. Amongst males 20-24, mortality estimates were similar to the EU15+ median in the UK and all constituent countries except Northern Ireland, where rates were higher. Within English regions, mortality rates only differed from the EU15+ median in London, where they were lower. 22 (14.7%) local authorities had estimates higher than the EU15+ median, and 49 (32.7%) local authorities had estimates

which were lower than the EU15+ median. Amongst females 20-24, mortality rates were similar to the EU15+ median in the UK, England and Wales, and higher in both Scotland and Northern Ireland. Within English Regions, mortality rates in the South West and West Midlands were higher than the EU15+ median, and those in North East, East Midlands, South East and London were lower than the EU15+ median. 29 (19.3%) local authorities had estimates higher than the EU15+ median and 41 (27.3%) had estimates lower than the EU15+ median.

Figure 34: All-cause mortality per 100,000 in 2017 in the UK, England, Northern Ireland, Scotland, Wales and the 9 Government Regions of England, compared with EU15+ countries by age group and sex



Notes: The size of each mark proportional to population
The horizonal red line indicates EU15+ median,
The pink horizontal lines indicate upper and lower 95% confidence intervals

Figure 35: All-cause mortality per 100,000 in 2017 in 1 to 4 year olds by sex in English Local Authorities compared with the EU15+ median (Greater London also shown separately)

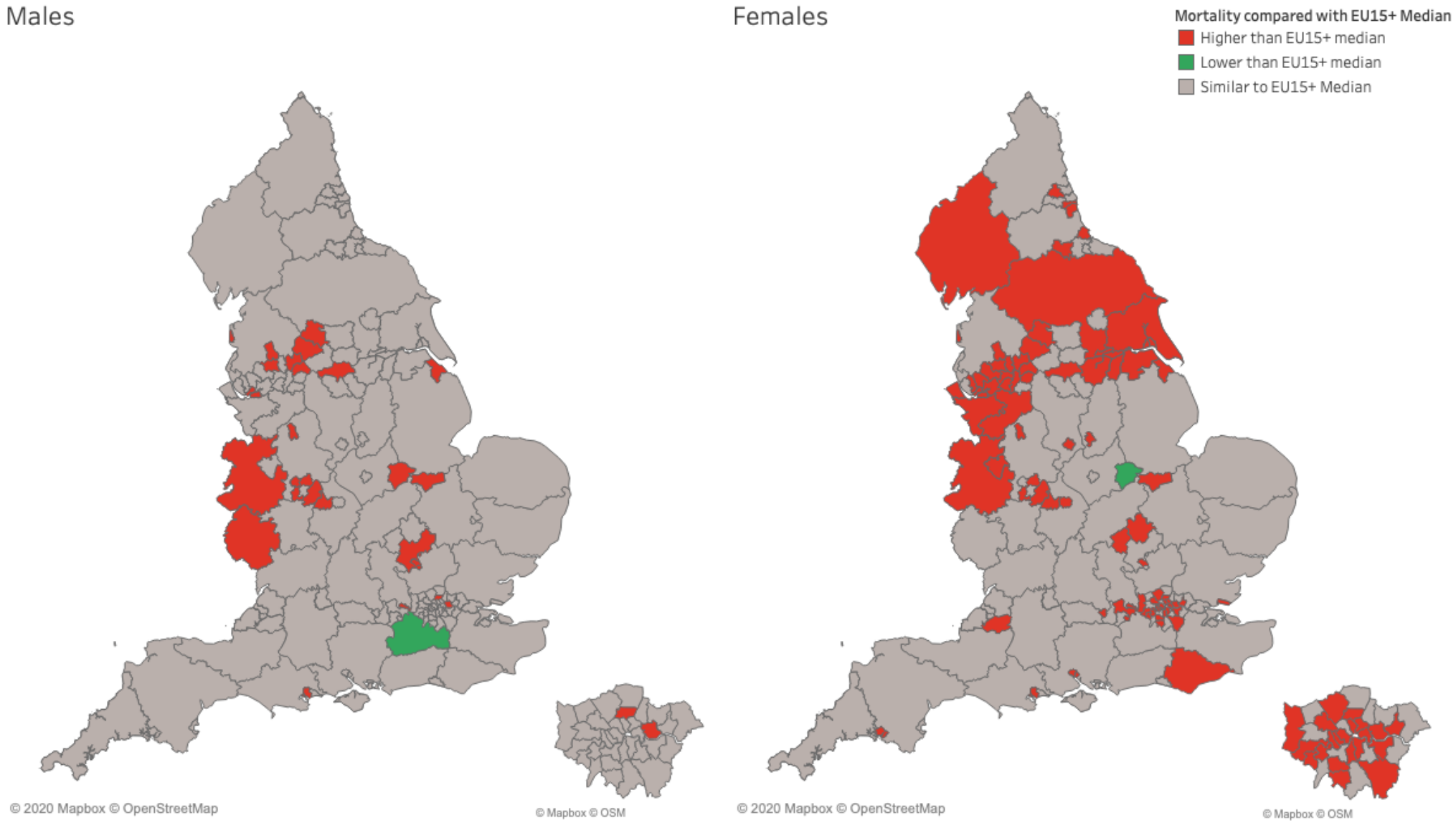
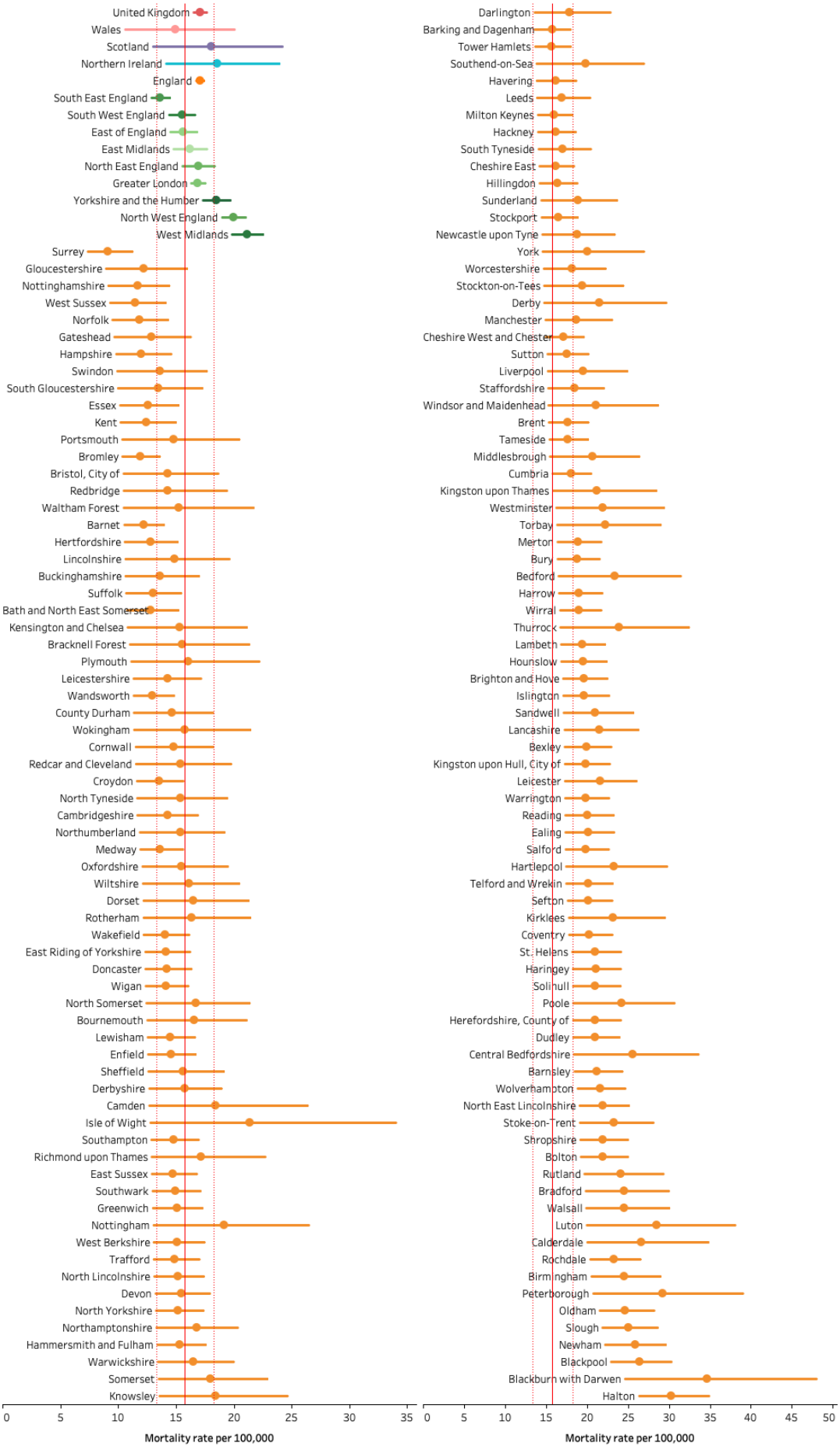
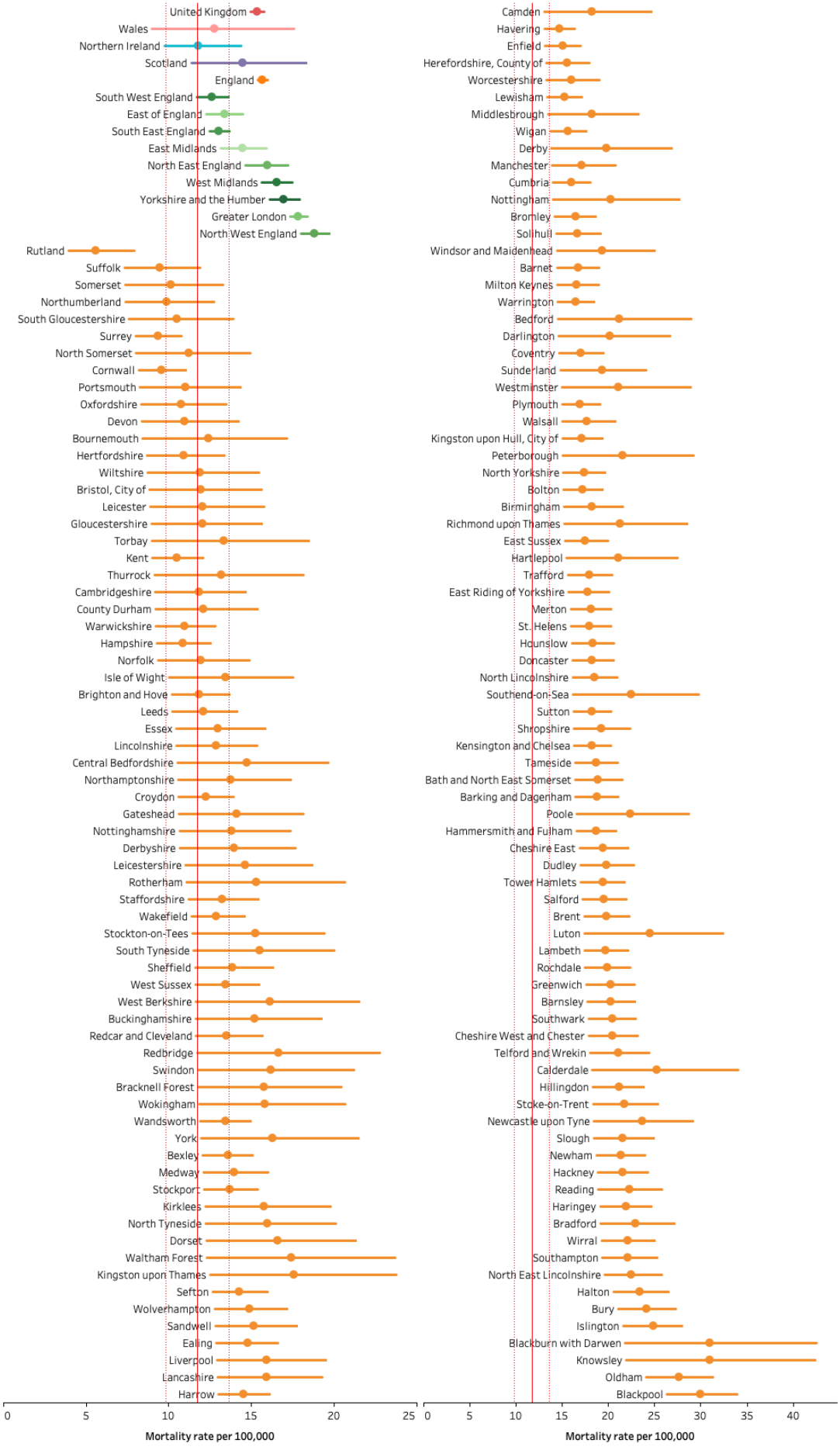


Figure 36: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 1 to 4 year old males in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 37: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 1 to 4 year old females in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 38: All-cause mortality per 100,000 in 2017 in 5 to 9 year olds by sex in English Local Authorities compared with the EU15+ median (Greater London also shown separately)

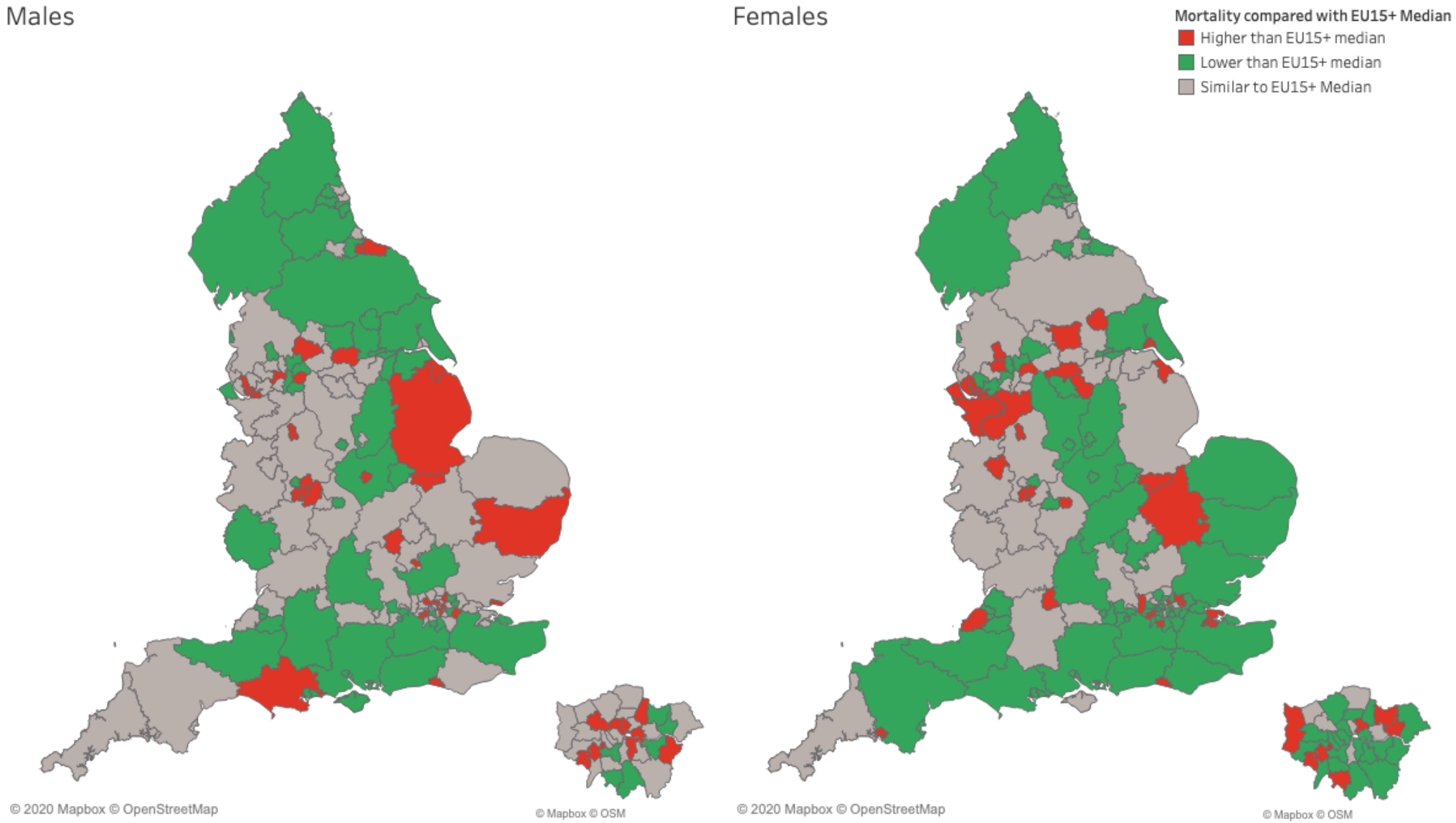
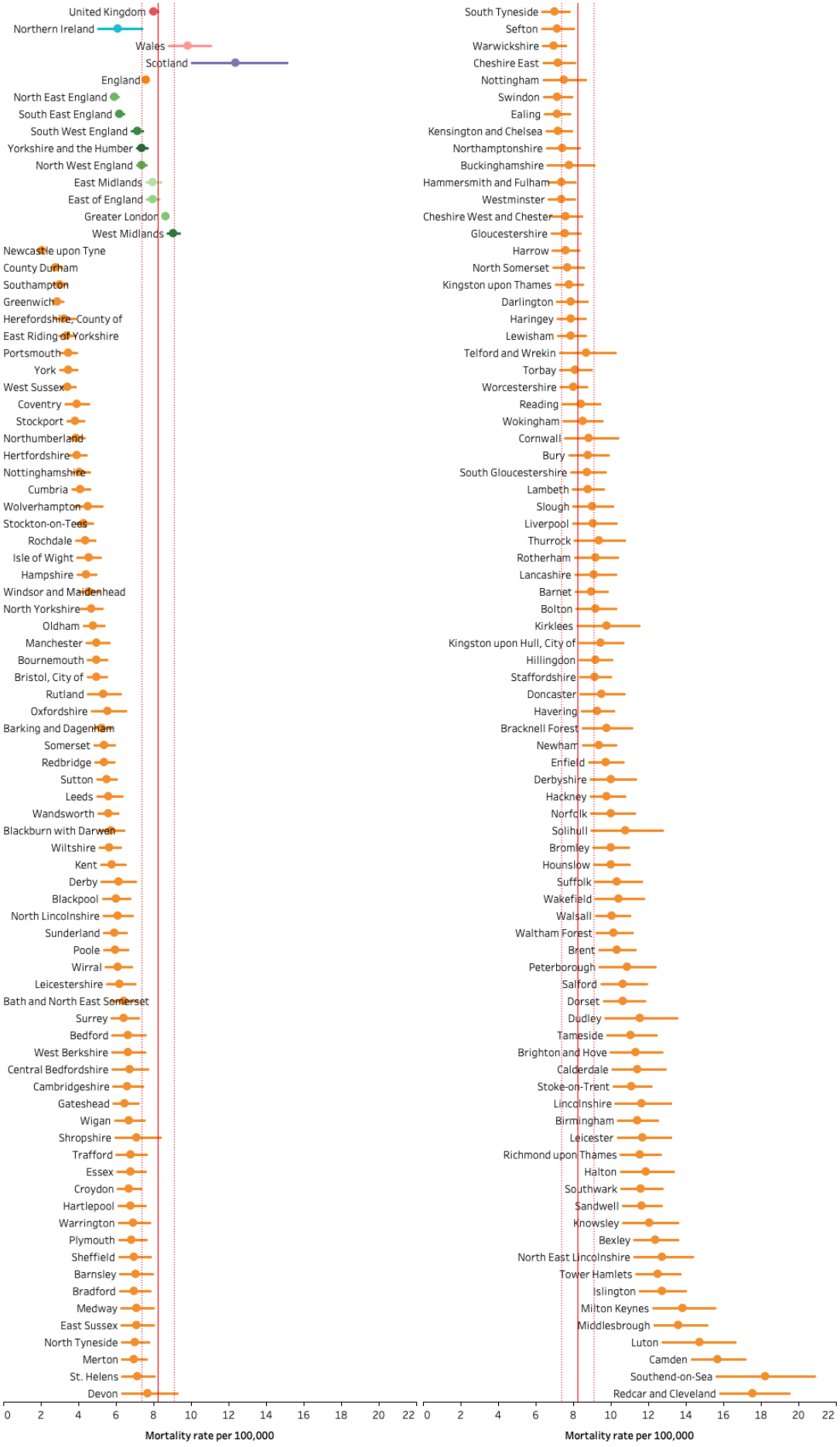


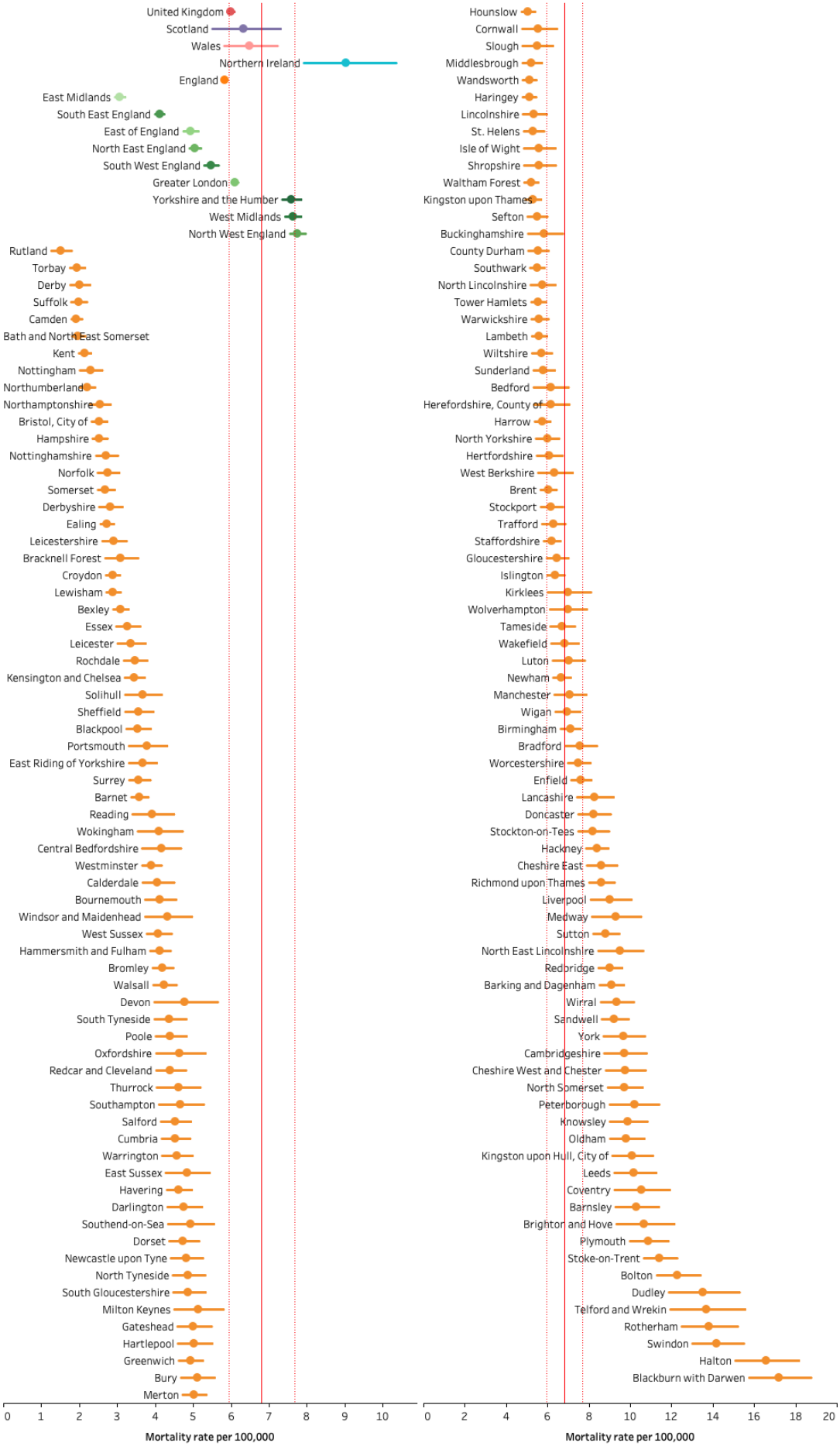
Figure 39: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 5 to 9 year old males in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]Hillingdon is excluded for clarity – mortality rate 25.65 [24.09-27.29]

[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 40: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 5 to 9 year old females in UK countries, English regions and English local authorities[i] compared with the EU15+ median.[ii]



[i]Hillingdon is excluded for clarity – mortality rate 25.65 [24.09-27.29]

[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 41: All-cause mortality per 100,000 in 2017 in 10 to 14 year olds by sex in English Local Authorities compared with the EU15+ median (Greater London also shown separately)

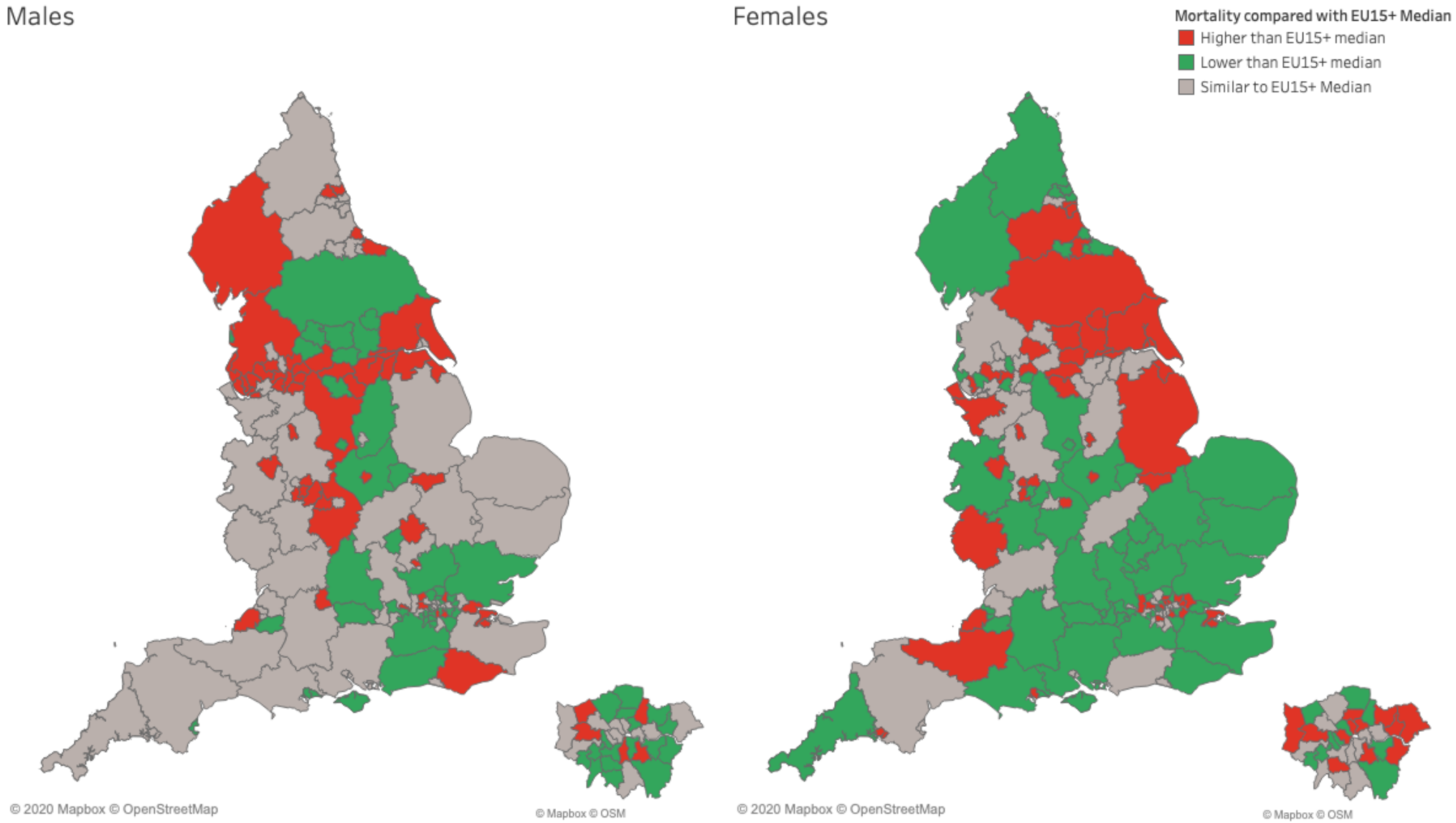
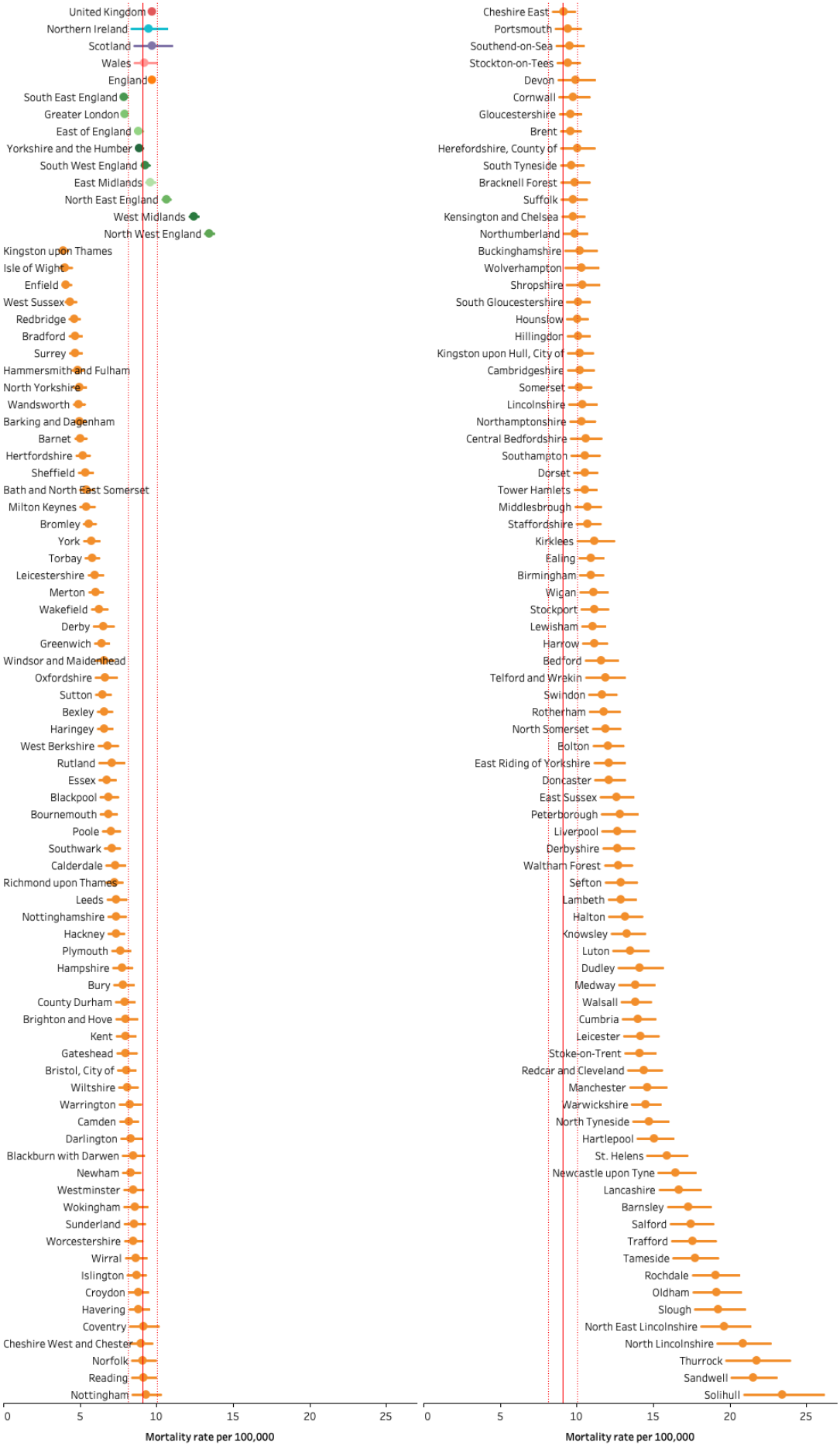
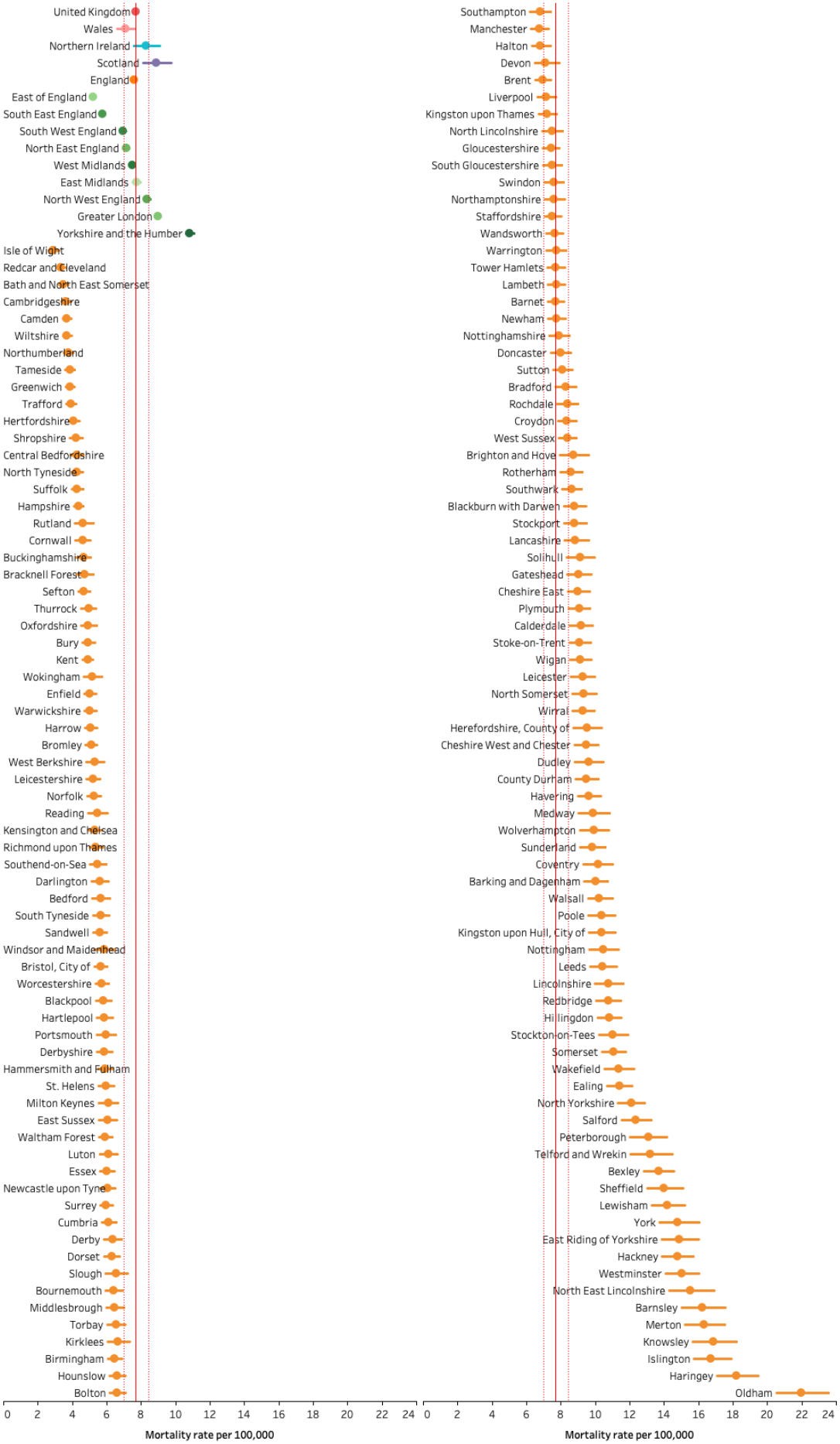


Figure 42: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 10 to 14 year old males in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 43: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 10 to 14 year old females in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 44: All-cause mortality per 100,000 in 2017 in 15 to 19 year olds by sex in English Local Authorities compared with the EU15+ median (Greater London also shown separately)

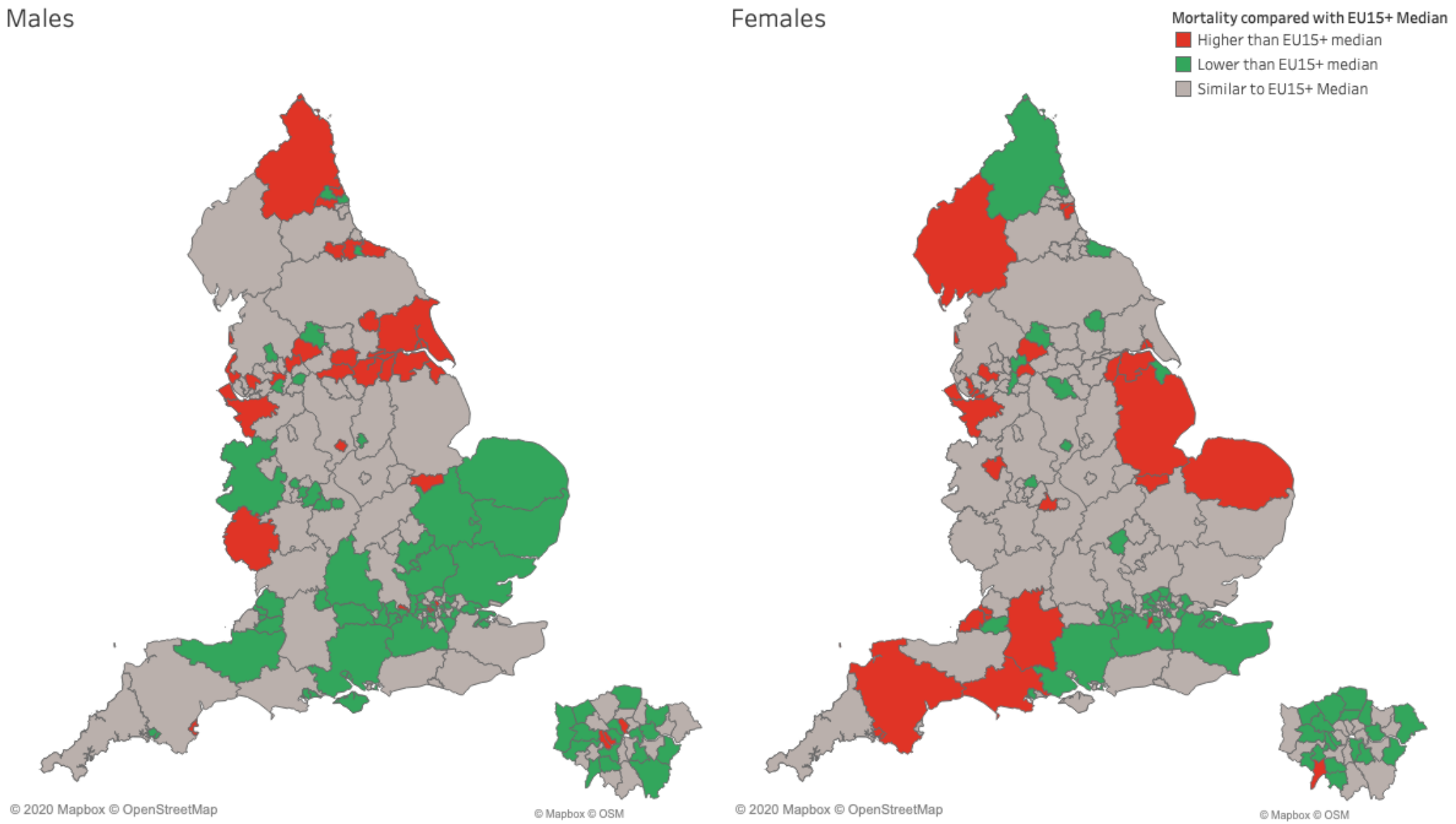
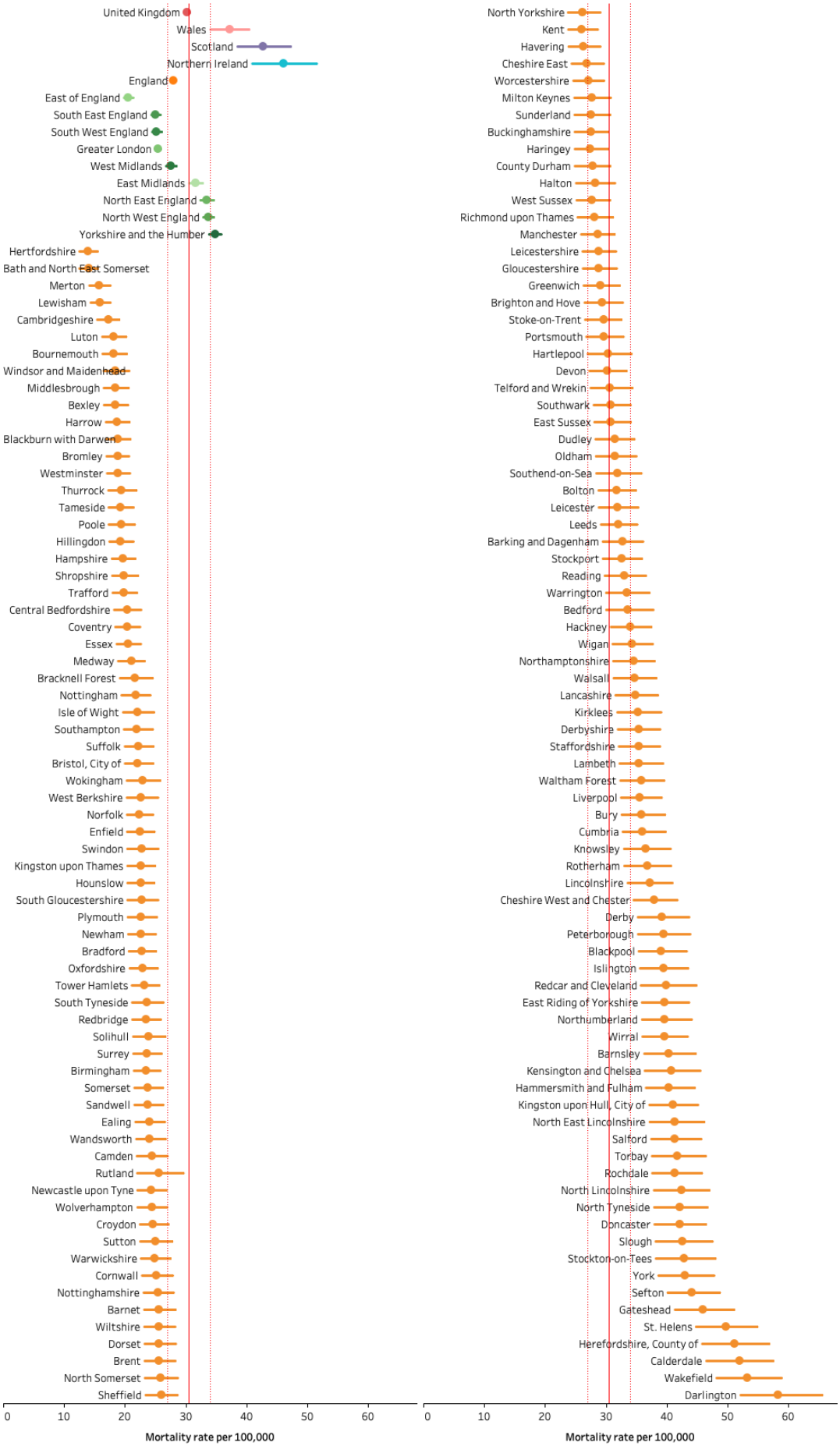
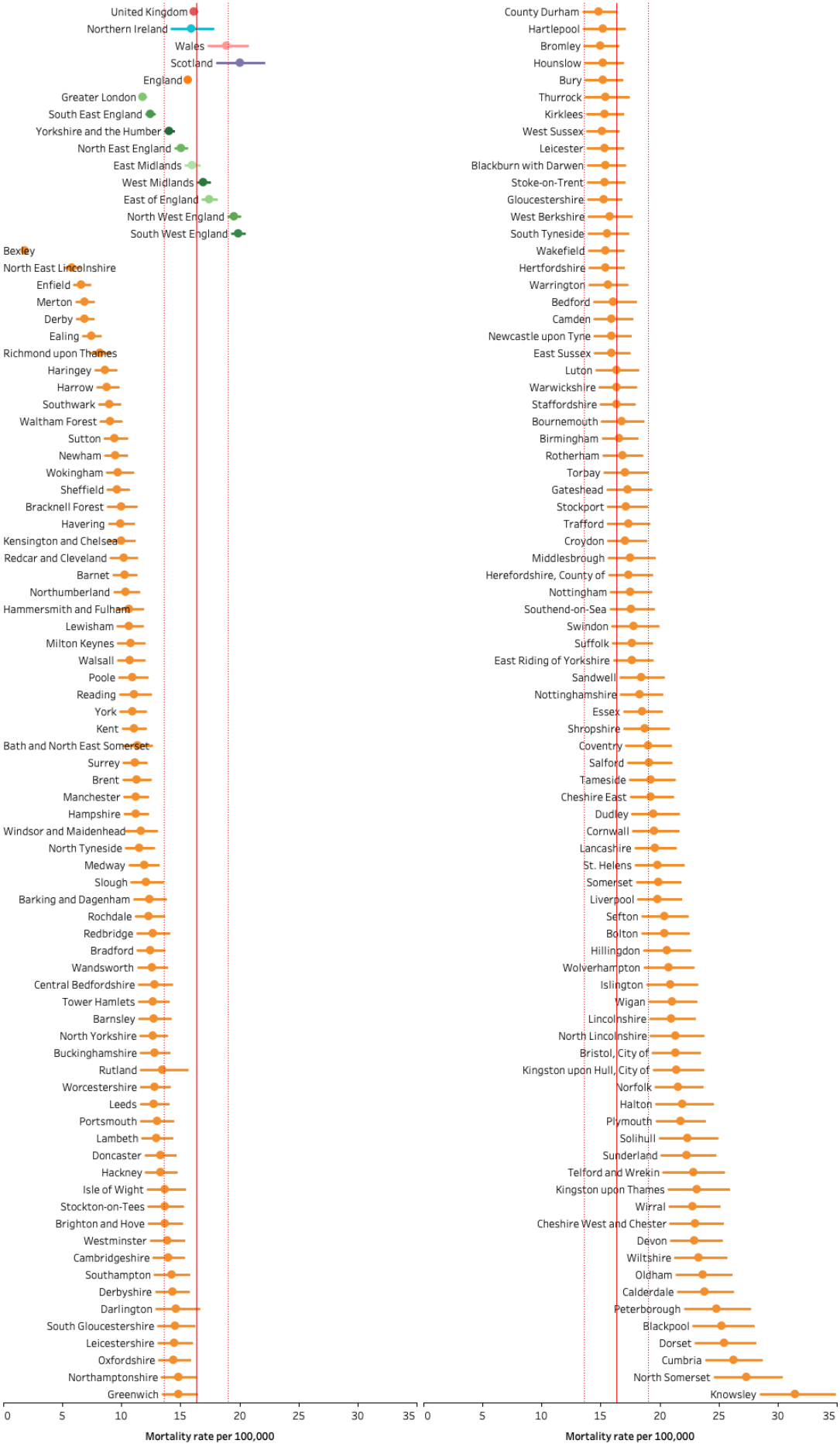


Figure 45: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 15 to 19 year old males in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 46: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 15 to 19 year old females in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 47: All-cause mortality per 100,000 in 2017 in 20 to 24 year olds by sex in English Local Authorities compared with the EU15+ median (Greater London also shown separately)

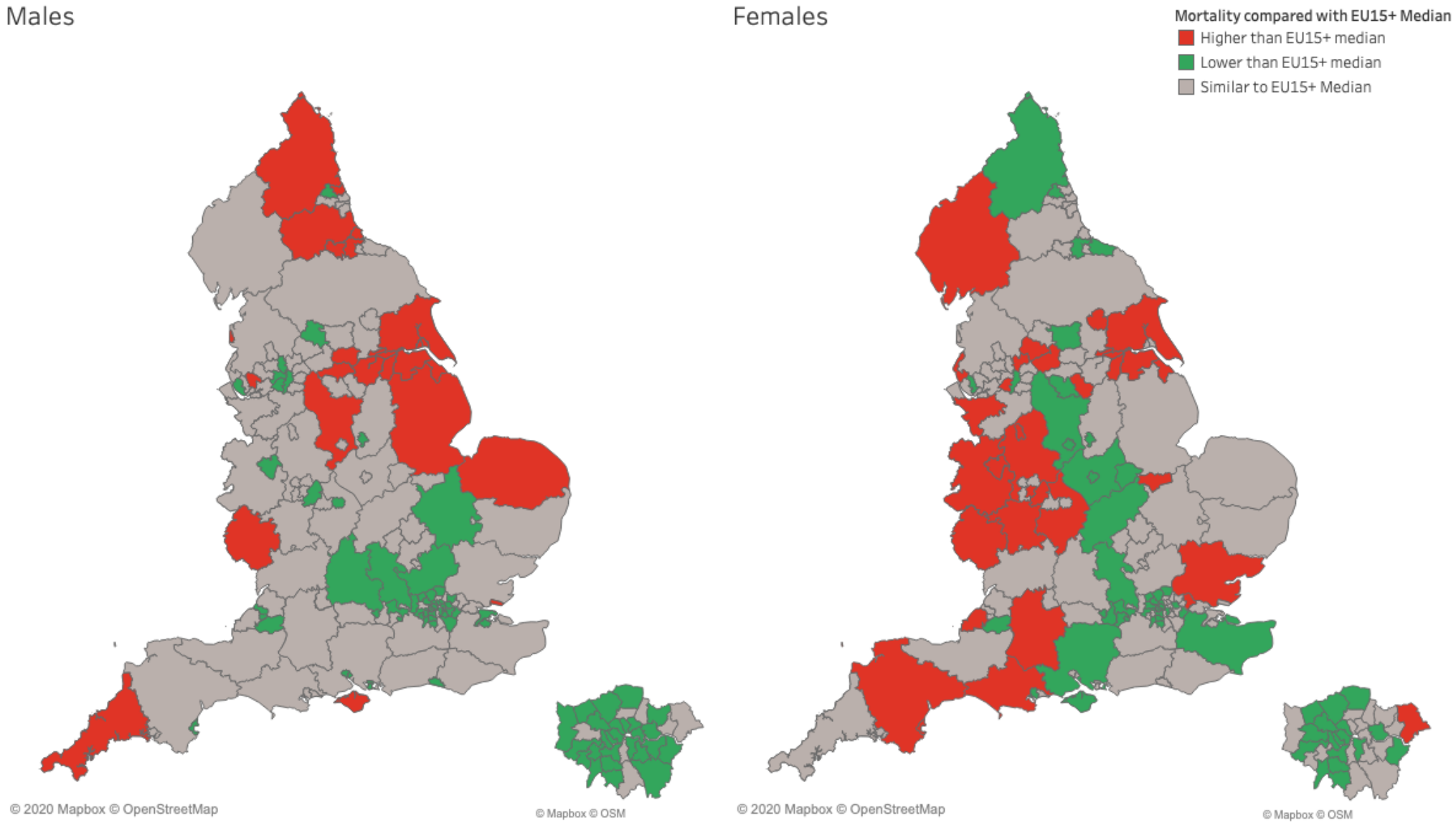
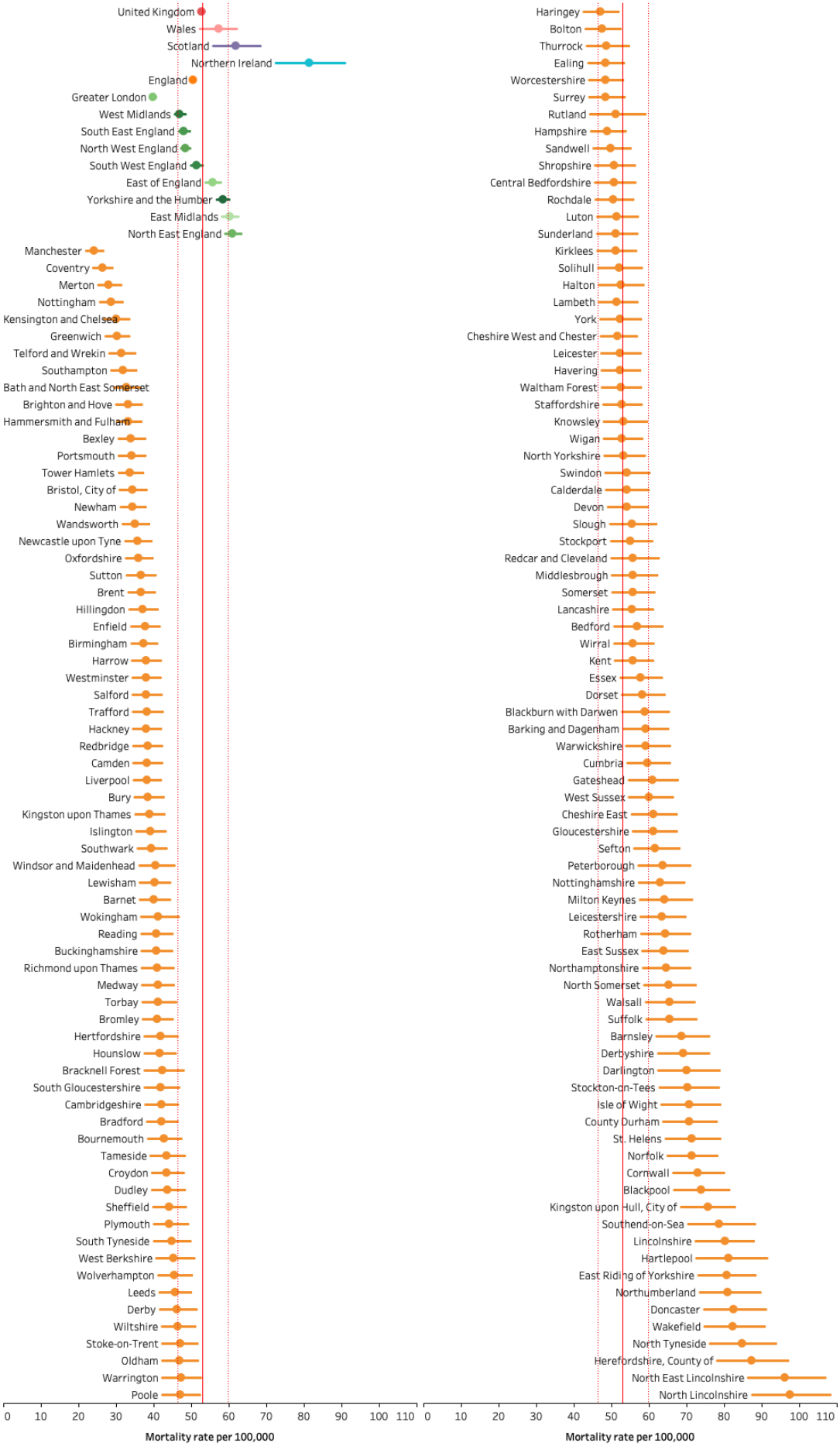
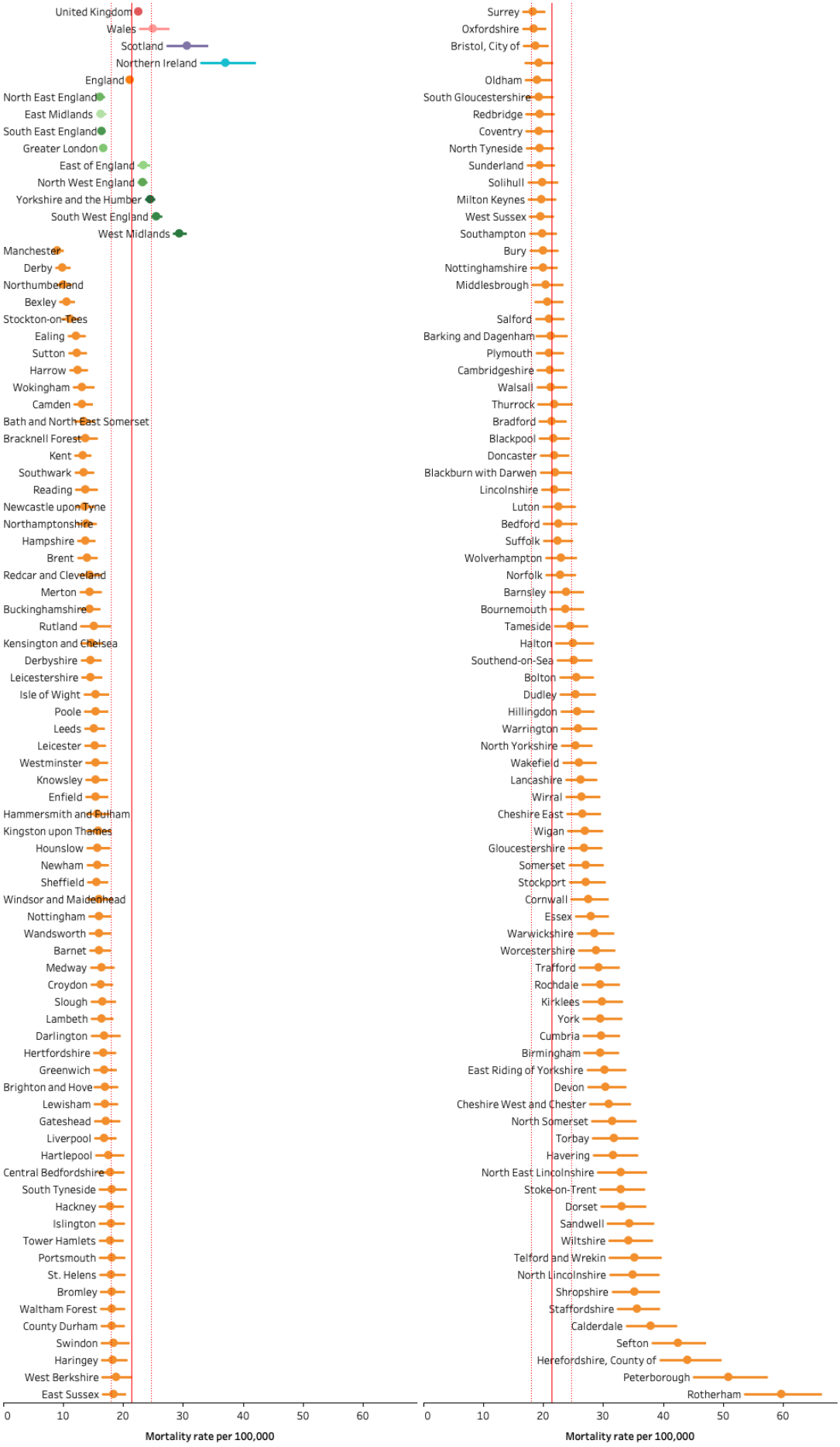


Figure 48: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 20 to 24 year old males in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines.

Figure 49: All-cause mortality rate per 100,000 with upper and lower uncertainty bounds in 2017 in 20 to 24 year old females in UK countries, English regions and English local authorities compared with the EU15+ median.[i]



[i]The EU15+ median is shown as a red vertical line, with upper and lower 95% confidence intervals shown as red vertical dashed lines

Chapter 5 discussion

These findings show wide sub-national variation in CYP mortality within the UK, with contrasting patterns between age groups, sex, and causes of death. Overall, I found all-cause mortality for CYP to be lower in England than other parts of the UK, and within England outcomes are generally better in the South and South East. High mortality in Scotland and Northern Ireland for leading causes of death in 15-24 drive wide differences in outcomes compared to England. However, for young children, mortality in England is similar to or worse than the rest of the UK, driven by poor outcomes for infectious causes of death.

These findings are similar to previous work showing mortality in CYP to be lower in England than other parts of the UK. The recent RCPCH State of Child Health report demonstrated all-cause mortality in 2017 amongst 1-9 year olds to be highest in Northern Ireland, and outcomes for 10-19 year olds to be worse in Scotland and Northern Ireland compared with England and Wales.[9] Using data from a decade prior to this, Northern Ireland was also identified as having high mortality compared with other regions of the UK in the Confidential Enquiry into Maternal and Child Health (CEMACH).[59] England has also been shown to have higher life expectancy than Scotland and similar to Wales and Northern Ireland.[212] Within England, variation between the 9 government regions has also been described, with worse outcomes in the Midlands and north of England compared with the south and east.[59,203] Sidebotham et al. found the exception to this to be the North East of England, where outcomes were around the best in England in an analysis using data from 2009-2011, although this was only significant for infants and not older children.[203] At local authority level, the Atlas of Variation in Healthcare for Children and Young people (2016)[62] demonstrated differences in all-cause mortality using data from 2002-2012. Similar to my findings, the authors found a 5.5 fold difference between worst and best performing local authority for directly standardized all-cause mortality amongst 1-17 (both sexes), and showed some evidence this variation is increasing.[62]

Similar to my findings, previous work has shown the causes of death driving large differences in CYP mortality outcomes between England and the other UK countries to be those related to drug use, self-harm and injuries. Hardelid et al. found lower mortality due to injury in 1-18

year olds in England compared with the other UK nations, and that this disparity increased from 1980 – 2010.[53] Differences noted between Northern Ireland and regions of England in CEMACH using data from 2006 were also found to be driven by excess deaths due to injury and self harm.[59] Within England, using data from 2002-2011 the Atlas of Variation in Healthcare for Children and Young People[62] showed there to be around a 6 fold range in accidental injury mortality between local authorities, with the North West of England having worse outcomes than the areas of the South and East. Notably, variation in mortality due to external causes will disproportionately affect adolescents and young adults, as these are the predominate causes of death in this age group (described in Chapter 3).

The results shown here may aid interpreting UK CYP mortality performance compared with similar countries. In 1-4 year olds, although the UK and England have similar all-cause mortality to the EU15+ median, the mortality rate for both sexes in the West Midlands and North West are higher than any EU15+ country. At the local authority level, only 1 local authority had an all-cause mortality rate which was significantly lower than the EU15+ in either sex in this age group, and amongst females 50% of local authorities had significantly higher mortality than the EU15+ median. Some of the largest differences in mortality rates within the UK are seen in older adolescents 15-24, with Scotland and Northern Ireland emerging as areas of the UK with particularly high mortality compared with the EU15+. Although as a whole, UK all-cause mortality is similar to the EU15+ in this age group, this conceals these differences, particularly for Northern Ireland, which has a higher point estimate for all-cause mortality in 20-24 than any EU15+ country. Cause specific variation in the UK may add further insights to explain differences compared to the EU15+. The results in this chapter show that some of the largest subnational differences in outcomes occur in conditions where I found UK mortality to be higher than the EU15+ in Chapter 4, including infectious causes of death (1 to 4 and 5 to 9 year olds), asthma (5 to 9 and 10 to 14) and epilepsy (5 to 9). Improving outcomes in these conditions, and so reducing differences between the UK as a whole compared with the EU15+, will require focus in these areas.

Strengths and weaknesses

These analyses provide a comprehensive description of variation in CYP mortality within the UK. I am not aware of any previous work to describe variation in local authority mortality in CYP which also disaggregates by 5-year age group and cause of death in 1-24; previous studies at local authority level have analysed trends in infant mortality,[213] grouped older CYP 1-17, or focused on specific causes.[62] However, the methods described here are subject to a number of limitations. I have chosen to focus on current differences in CYP mortality, and have not analysed subnational trends over time, which may provide additional insights. Small numbers of deaths in some age groups, causes and regions of the UK result in large year-on-year variation which may result in differences in country and local autority mortality rank. As IHME do not provide uncertainty intervals for the EU15+ group of countries, I have estimated confidence intervals using uncertainty bounds within each country, and so interpreting comparisons between the EU15+ and subnational UK mortality should be viewed in this context. Finally, although the data used here are based on death registration, they are also modelled and so subject to limitations within the GBD estimation process.[205] Effects of using modelled data can be substantial and are not confined to data-poor settings; using other data sources may have made large differences to my results. Rigby et al. compared all-cause mortality estimates and mortality rank for 10-14 year olds within 30 European countries using Eurostat and GBD data. They found estimates to differ for each country, and for only two to have a common rank using both datasets.[191] However, alternative sources of data which provide the level of geographic granularity described here are sparce. Analysing patterns of death by local authority using ONS death certificate data is not possible due to restrictions on releasing fields with low counts, and although Public Health England do provide estimates for CYP mortality by local authority, these data group CYP 1-17 and are not available by cause of death.

Conclusions

These results provide a framework to focus attention on parts of the UK with the highest mortality outcomes for CYP, which are likely to be contributing most to the UK's poor international performance. They also demonstrate that large parts of the UK have mortality rates which are comparable with the best performing countries in the EU15+, particularly in school age children and adolescents, highlighting the potential for improvement in the UK as

a whole. Exploring the mechanisms behind variation described here requires an understanding of how determinants of CYP health and survival vary.[62] Demographic and socioeconomic factors are fundamental to this, and in the next chapter I will explore the extent to which geographic differences in CYP mortality in England can be explained by ethnicity, deprivation, and population structure within local authorities.

Chapter 6

Understanding demographic, socioeconomic and regional variation in child and young person mortality

In Chapter 5 I described large geographic variation in CYP mortality within the four countries of the UK, and within England by region and local authority. Understanding these differences requires exploring variation in key determinants for CYP mortality. Among the most important of these is socioeconomic deprivation, previously shown to be strongly associated with CYP mortality in multiple studies[12,19,25,27-39] and highlighted in the RCPCH reports *Why Children Die*[13] and the *State of Child Health* 2017 and 2019.[12,55,77] In order to assess the extent to which socioeconomic factors are contributing to excess UK CYP mortality, it is important to assess associations across age groups in 1-24. Although social gradients in mortality have been described throughout the early life course, some studies have shown the effect of deprivation to weaken during adolescence, although the evidence for this is mixed.[29,36,214] This may reflect variation in patterns of causes of death between young children and adolescents, but also changes in the mechanisms through which socioeconomic factors operate.

In this chapter I will examine how geographic variation in CYP mortality may be explained by socioeconomic and demographic factors, and compare this by age group. I will do this in two parts. First, I will explore national trends in CYP mortality in England by individual/family level socioeconomic status using National Statistics Socioeconomic Classification (NS-SEC), and area level deprivation using Index of Multiple Deprivation (IMD) quintile category. Secondly, I will describe how variation in CYP mortality between English local authorities in 2017 is associated with deprivation score, a population weighted metric based on IMD rank within each local authority. Observed associations between local authority deprivation may be confounded by other area level determinants of mortality, including demographic factors and population ethnicity. CYP from diverse ethnic minority groups have previously been identified as having increased mortality risk,[43-50] and the age structure of local authorities is also likely to be associated with variation in outcomes, as local authorities with younger populations may have greater focus on the health needs of CYP. To account for this, I will examine associations between local authority deprivation and all-cause mortality, adjusting for the

proportion of local authority population which is of minority ethnic groups, and the proportion of the local authority population which is aged 1-24. Finally, I will examine the extent to which differences in all-cause CYP mortality between English local authorities can be explained by geographic clustering within Region, and how this varies across age groups.

Chapter 6 methods

Data

Deprivation

National Statistics Socioeconomic Classification (NS-SEC)

I analysed variation in CYP mortality in England by individual / family level socioeconomic group using National Statistics Socioeconomic Classification (NS-SEC) code. These data are recorded on death certificates as described in Chapter 2, and were extracted from *Office for National Statistics. (2019). Death Registrations in England and Wales, 1993 – 2018: Secure Access. [data collection] 5th Edition. UK Data Service. SN:8200*.

NS-SEC is an 8-level occupation-based classification system which has been constructed to measure employment relations and conditions of employment. I collapsed these into three occupation groups as described by the Office for National Statistics (ONS).[215] These were: Managerial occupations (analytic codes 1,1.2,2) Intermediate occupations (3,4) and Manual occupations (5,6,7). I chose to exclude CYP / families in NS-SEC group 8 (not employed, full time students, not classified for other reasons) from these analyses, due to concerns around interpreting these categories and the reliability of population denominators for these groups. Due to restrictions on releasing estimates with low numbers from the UK Data Service Secure Lab (where these data are held), these results are presented for both sexes.

Index of Multiple Deprivation

I defined area level deprivation within England using Index of Multiple Deprivation (IMD) quintile category. IMD is a measure of relative deprivation by Lower Super Output Area (LSOA); a small geographic area with a population of between 1000 to 3000 people (mean

1500) and containing between 400 and 1200 households.[216] IMD is based on indicators of deprivation within seven domains: income deprivation; employment deprivation; education, skills and training deprivation; health deprivation and disability; crime; barriers to housing and services; living environment deprivation.[217] Indicators within each domain are combined or aggregated to obtain a score for that domain. Each domain is then weighted to obtain a summary index.[218] The income and employment domains are given weights of 22.5%, health and disability, and education training and skills domains 12.5%, and barriers to housing and services, living environment, an crime dimension 9.3%.[218] Although indicators within each domain have been modified with iterations of the IMD since its inception in 2000, the fundamental methodology, spatial unit, domain number, and domain weights, have not changed since 2004.[217,219] There were no changes made to IMD between IMD 2010 and IMD 2007, and only minor changes to the indicators in IMD 2015.[220] However, as IMD 2010 and IMD 2015 span the 2011 census, this may have some effect on estimated levels of deprivation due to revised population denominators and modifications to geographic boundaries, which affected around 2.5% of LSOAs.[220] I used estimates for number of deaths and population denominators in England for IMD 2004 for data years 2001 – 2005, IMD 2007 for data years 2006 – 2008, IMD 2010 for data years 2009 – 2012 and IMD 2015 for data years 2013 – 2018.

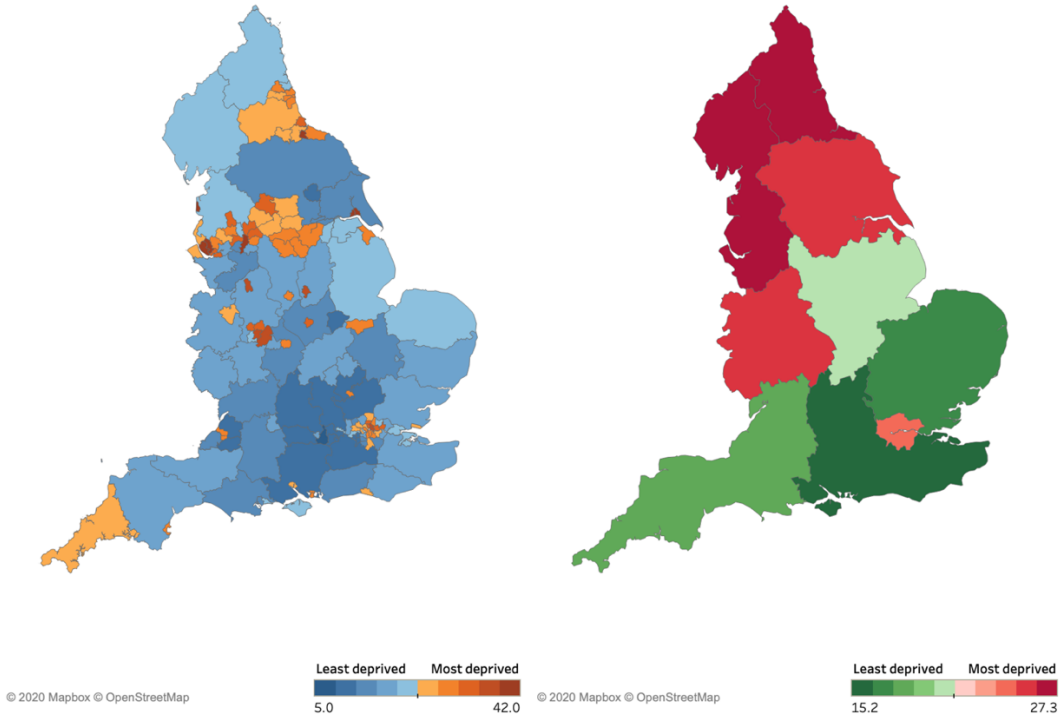
Local Authority Index of Multiple Deprivation Score

I used IMD 2015 to estimate a population weighted deprivation score for each English local authority in 2017. I used data for IMD within each of 32,845 LSOAs in England, provided by the UK Ministry of Housing, Communities and Local Government, and downloaded from www.gov.uk on 29th Jan 2020. I mapped these to the 150 local authority locations used by the Global Burden of Disease (GBD) study (described in Chapter 5), and then to the 9 English Regions, using either lower or upper tier local authority codes available here: https://data.gov.uk/dataset/4b324283-7091-413c-b9a1-5dd388e15306/lower-tier-local-authority-to-upper-tier-local-authority-december-2017-lookup-in-england-and-wales. The number of LSOA within each local authority ranged from 23 (Rutland) to 902 (Kent). I calculated the average IMD score within each local authority, weighted by 2017 mid-year total population estimates within each LSOA, using methods described in the English Indices of Deprivation 2015.[220] I then repeated this methodology to estimate a population weighted

IMD score for each English region. In addition, I calculated the proportion of LSOA within each local authority which were within the most deprived 10% and 20% nationally, as an alternative measures of deprivation at local authority level.[221]

The local authority population weighted IMD score ranged from 5.61 in Wokingham (least deprived) to 42 in Blackpool (most deprived); the English region population weighted IMD score ranged from 15.2 in South East (least deprived) to 27.3 in North West (most deprived) (see figure 50). The proportion of LSOA within each English region which were in the most deprived decile category nationally were South East 3.0%, East of England 4.1%, South West 4.8%, London 5.7%, East Midlands 11.6%, West Midlands 15.4% North East 17.1%, Yorkshire and the Humber 18.1% and North West 19.6%. The top five local authorities with the highest proportion of LSOAs in the most deprived decile were in the North East (Middlesbrough, 48.8%), the North West (Knowsley 45.9%, Liverpool 44.8%, Manchester 40.8%) and Yorkshire and the Humber (City of Kingston upon Hull 45.2%). 18 (12%) of local authorities had no LSOAs in the most deprived decile nationally.

Figure 50: Weighted IMD score within 150 English local authorities (left) and within the 9 English government regions (right)



Mortality

I requested estimates for number of registered deaths in England from all causes by IMD quintile category and year of age (1-24) between 2001 – latest available (2018) from ONS. These are now publicly available, and downloaded on 23rd Jan 2020 from www.ons.gov.uk. Deaths from all causes by NS-SEC (with population denominators) were available from 2002 – 2016, and extracted from *Office for National Statistics. (2019). Death Registrations in England and Wales, 1993 – 2018: Secure Access. [data collection] 5th Edition. UK Data Service. SN:8200*

I used the same mortality data at local authority level provided by the Institute of Health Metris and Evaluation (IHME) as used in Chapter 5. These were estimates for mortality rate per 100,000 with uncertainty intervals in 150 upper tier English local authorities in 2017. Data were provided by sex in 1-4, 5-9, 10-14, 15-19, 20-24, for all-causes in 2017.

Population

Estimates for population of England by 5-year age group, sex, IMD quintile from 2001 – 2018 and by NS-SEC group 2002 - 2016 were requested from ONS, and are now publicly available from www.ons.gov.uk.

Local authority population estimates for 2017 were routinely available and downloaded from ONS. This ranged from to 1,554,636 in Kent to 39,474 in Rutland. The population of 1-24 year olds ranged from 10,176 in Rutland to 455,184 in Kent. The proportion of the total population who were aged 1-24 ranged from 23.4% in Dorset to 39.4% in Nottingham.

Ethnicity

Local authority population estimates by ethnicity for 2016 were also downloaded from ONS, and derived from the Annual Population Survey (2016) and UK census (2011).[162] These data are not official statistics, but were created by ONS to calculate population estimates by ethnicity for the years between each census. The six ethnic groups used by ONS are White British, All Other White, Mixed, Asian, Black and Other. I analysed variation in CYP mortality between local authorities by the proportion of the total population that was Black, Asian and

Minority ethnic (BAME) groups (Mixed, Asian, Black or Other). BAME is a term commonly used to describe diverse minority ethnic groups in the UK, but has recently been criticised for equating ethnicity with skin colour and combining diverse populations with one term.[222,223] The term BAME also overlooks variation in health outcomes between diverse ethnic groups, (and in their experience of racism), and excludes minority White ethnic groups who also experience poor health, (such as Roma, Gypsy and Traveller groups).[223] However, I have chosen to describe variation in ethnicity within local authority using the term BAME for brevity and due to low numbers of deaths in CYP within more granular definitions, but do so acknowledging these limitations.

Rutland had a BAME population estimate which was less than 500 (i.e. rounded to zero), and was excluded from the regression analyses. The range in the remaining local authorities was 1.1% in Hartlepool to 66.3% in Newham. 25 out of the top 30 local authorities for BAME population (i.e. the top quintile category) were in Greater London; the remainder were Manchester, Birmingham, Leicester, Slough and Luton

Analyses

Describing individual variation in child and young person mortality by socioeconomic group in England

I first describe differences in mortality rate per 100,000 in CYP England by IMD quintile category between 2001 to 2017 and by CYP NS-SEC group between 2002 to 2016, using three year lagged mean mortality rates (because of high year-on-year variation in deaths). I calculated 95% confidence intervals around mortality rates within each NS-SEC group and IMD quintile using the *statsby varnames: ci* command in STATA. I calculated the percentage difference in three year lagged mean mortality rate in CYP living in the most deprived IMD quintile category compared with the least deprived quintile category, and amongst CYP where parents of the deceased were classified as in "Managerial" occupations compared with those classified as "Manual" using NS-SEC. I then used population denominators within each IMD quintile category and the three-year lagged mean mortality rate in the least deprived category, to calculate the annual number of deaths in England had all CYP had the same mortality rate as those in the least deprived category.

Describing variation in child and young person mortality by deprivation between local authorities

I assessed associations between local authority deprivation and CYP mortality using similar methods to those described by Steel et al, who also used GBD data to describe patterns of mortality in older groups by English local authority.[205] I compared the all-cause CYP mortality rate in the 10 most deprived local authorities and the 10 least deprived local authorities with the mortality rate for England, and considered these to be significantly different from one another if uncertainty intervals provided by IHME did not overlap, (using methods similar to those in Chapter 5 to describe geographic variation in mortality). Note that as mortality data within the GBD are already smoothed, I did not use lagged mean mortality rate for this analysis, (as was required for the IMD and NS-SEC data above).

Linear regression models

I then assessed associations between all-cause mortality rate and local authority socioeconomic, demographic and geographic characteristics using linear regression models. All-cause mortality rate by age and sex group in 2017 was the dependent variable, and local authority IMD score, the proportion of population who were BAME, the proportion of the population aged 1-24, and English region were predictors in each model. I assessed if both continuous dependent and independent variables were normally distributed using histograms (Figure 51, p.180). Local authority CYP mortality rate and the proportion of the population who were BAME were included in regression models on a log scale due to non-normal distribution. English region was included as a factor variable, with the baseline group as the region with the lowest all-cause mortality rate within that age and sex group.

Collinearity assessment

One of the assumptions of linear regression models is that there is little or no co-linearity between predictors in the model. I assessed this using scatter plots, Pearson's correlation coefficients and variance inflation factors. Figure 52 (p.181) shows scatter plots of associations between the predictor variables included in the model (proportion BAME, local

authority IMD score and proportion population aged 1-24). Higher proportion BAME in the population was associated with higher local authority IMD score (more deprived) ($r=0.21$, $p=0.011$) and higher proportion of population aged 1-24 ($r=0.64$, $p<0.001$). Increased local authority deprivation was associated with higher proportion of the population aged 1-24 ($r=0.45$, $p<0.001$). The variance inflation factors (VIF) for these predictors were 1.83 for IMD score, 4.57 for proportion BAME and 3.00 for proportion aged 1 to 24. As all Pearson's coefficients were less than 0.8, and the variance inflation factors were all <10, I considered there to be only limited evidence of problematic collinearity using these predictors.

Assessment of model fit

Each predictor was assessed separately, before being added to the final model in a stepwise fashion. I assessed model fit using Akaike Information Criterion (AIC) and Bayesian Information Criterion (BIC). I compared nested models using likelihood ratio tests, to determine if the addition of covariates improved model fit. I then repeated the analysis using a mixed effect model, with a random effect for geographic region. I did this in order to calculate the intra-class coefficient (ICC), which I used to assess the variance in all-cause mortality within each age and sex group which can be explained by clustering within region, after adjusting for local authority socioeconomic and demographic factors.

Figure 51: Histograms of English local authority IMD weighted score, proportion BAME and proportion 1-24 in 2017

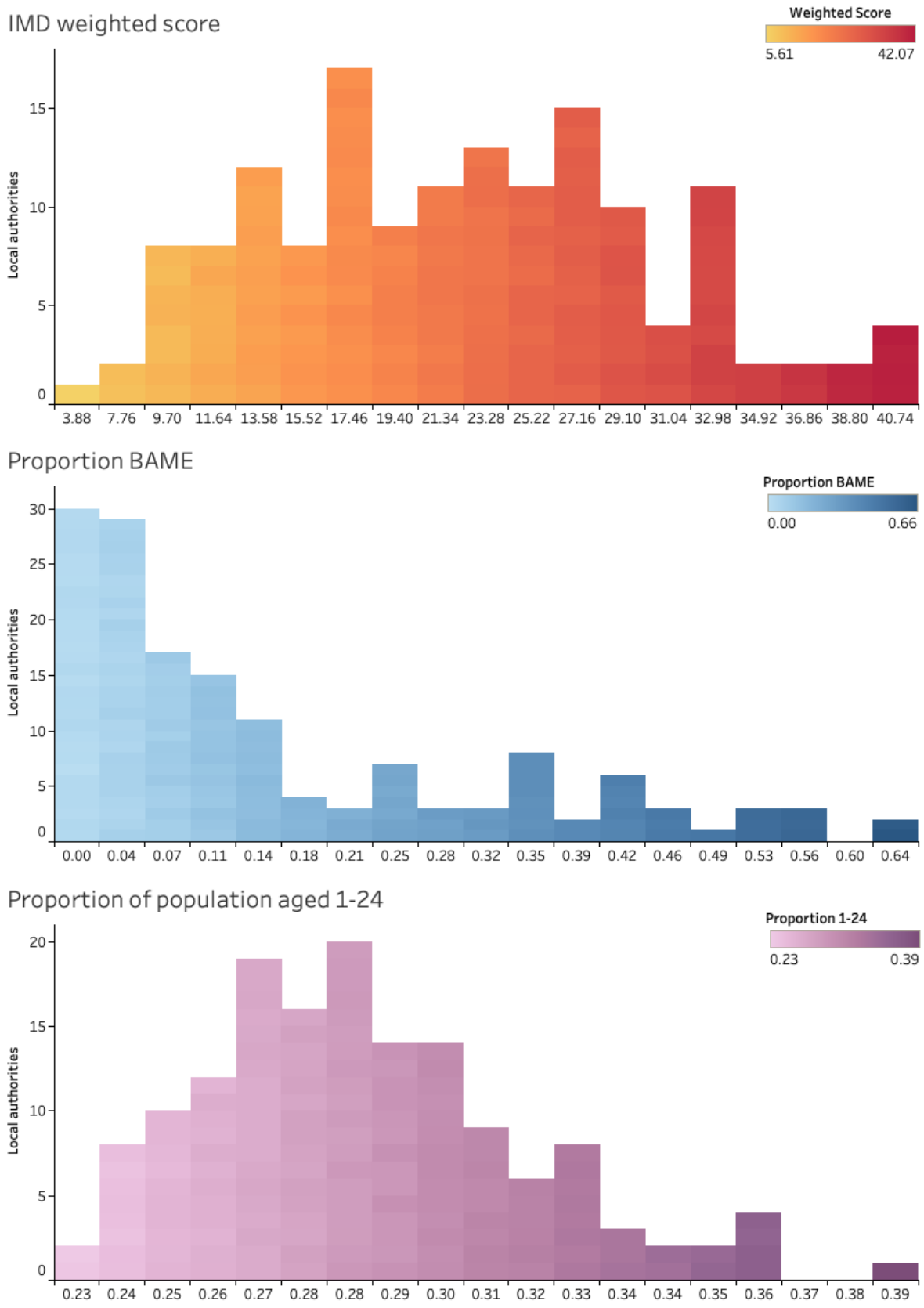
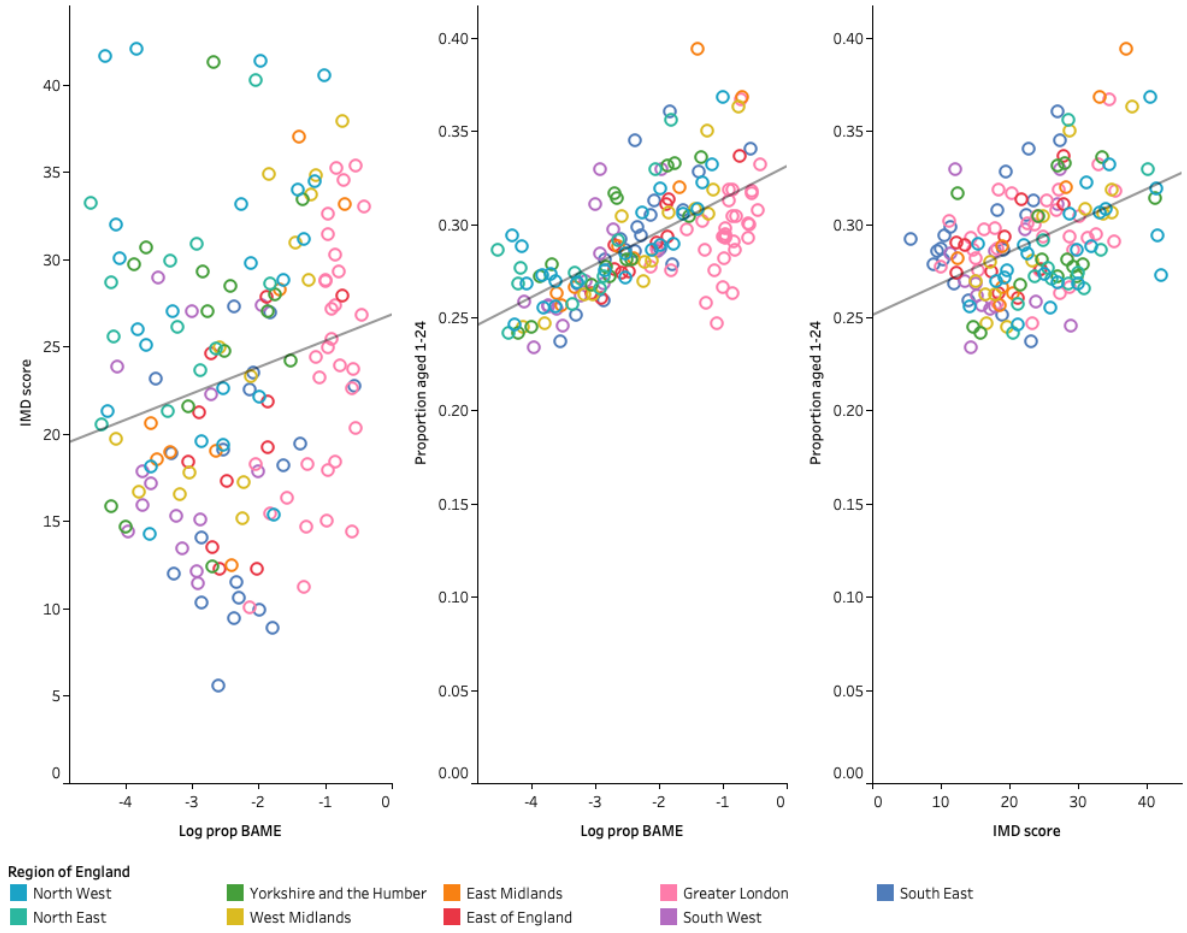


Figure 52: Associations between the proportion of the population BAME, IMD score, and proportion population aged 1-24 within English local authorities



Chapter 6 results

National variation in child and young person mortality by IMD

Figure 53 (p.185) shows the thee year lagged mean mortality rate by IMD quintile from 2001 – 2018, in 1-24 by 5-year age group for both sexes. In 2018, the three-year lagged mortality rate per 100,000 population amongst 1-24 was 62.8% higher amongst CYP in the most deprived quintile category (22.64 per 100,000 [95% confidence interval 21.15 – 24.20]) compared with those in the least deprived category (13.90 [12.57-15.24]). If the three-year lagged mean mortality rate for in 2018 for all CYP 1-24 was the same as that seen in the least deprived IMD category, around 600 deaths would have been avoided (around 21% of the total). Had this been the case over the previous ten years (2009 – 2018), around 7600 deaths would have been avoided.

In 2018, social gradients in mortality by IMD quintile category were evident in all age groups, and were steepest amongst 1-4 (table 19, p.184). Amongst 1-4 (both sexes), the three-year lagged mean mortality rate amongst the most deprived IMD quintile category was 19.83 [16.67-23.42], more than double that of the least deprived category, which was 9.76 [7.21-13.08]. In 5-9 year-olds, the three-year lagged mean mortality rate was 8.82 [6.94 – 11.05] in the most deprived quintile category compared with 5.07 [3.48-7.14] in the lease deprived category (74% higher). In 10-14 year-olds this was 11.74 [9.40-14.49] in the most deprived quintile category compared with 5.92 [4.18-8.15] in the least deprived (98% higher). In 15-19 year-olds this was 28.18 [24.37-32.41] in most deprived quintile category compared with 19.92 [16.56-23.75] in the least deprived (41% higher). In 20-24 year-olds this was 44.72 [40.26-49.54] in the most deprived quintile category and 30.66 [26.11-35.77] in least deprived in 20-24 (46% higher). Between 2001 and 2018, the difference between the three year lagged mean mortality rate in the most deprived IMD quintile category compared with the least deprived has remained fairly constant across all age groups except 10-14, where this has almost doubled from around 50% higher in the most deprived IMD category in 2001 to almost 100% higher in 2018.

National variation in child and young person mortality by NS-SEC

Figure 54 (p.186) shows the thee year lagged mean mortality rate by NS-SEC from 2002 – 2016, in 1-24 by 5-year age group for both sexes. Similar to the IMD analysis, there were steep social gradients in mortality across all age groups. Mortality rates were higher in CYP/families defined as in manual occupations compared with managerial occupations for all age groups. In contrast to variation in IMD, differences between mortality in manual occupations compared with managerial occupations were steepest in 15-24 year olds.

In 2016, within 1-4 year-olds, the mortality rate per 100,000 population within manual occupations was 19.03 [95% CI 16.21 – 22.19] compared with 11.21 [9.42 – 13.25] in managerial occupations (73.6% higher). Within 5 to 9 the mortality rate ranged from 10.36 [8.41– 12.62] in manual occupations compared with 5.55 [4.41 – 6.89] in managerial occupations (96.8% higher). In 10 to 14 this was 11.08 [8.91 – 13.62] in manual occupations and 7.1 [5.73 – 8.69] in managerial occupations (45.3% higher). In 15 to 19 this was 15.46 [12.98 – 18.29] in manual occupations and 3.45 [2.53 – 4.60] in managerial occupations (431.2% higher). In 20 to 24 this was 37.05 [33.50 – 40.86] in manual occupations and 9.87 [8.16 – 11.82] in managerial occupations (271.8% higher).

The difference in mortality rates between CYP in families of manual occupations compared with managerial occupations has been stable between 2002-2016 in most age groups, except 5-14 year olds, where this has doubled in both 5-9 and 10-14. Further, slow declines in adolescent and young adult mortality (15-24) described in Chapter 3 are more evident in manual and intermediate than in managerial occupations.

Table 19 All-cause mortality rate per 100,000 with 95% confidence intervals in the most deprived and least deprived IMD category, and manual and managerial NS-SEC category, by age group in 2017 in England (both sexes)

	IMD category			NS-SEC category		
	Most deprived	Least Deprived	Ratio	Manual	Managerial	Ratio
1 to 4	19.83 [16.67-23.42]	9.76 [7.21-13.08]	2.03	19.03 [16.21 – 22.19]	11.21 [9.42 – 13.25]	1.69
5 to 9	8.82 [6.94 – 11.05]	5.07 [3.48-7.14]	1.73	10.36 [8.41– 12.62]	5.55 [4.41 – 6.89]	1.86
10 to 14	11.74 [9.40-14.49]	5.92 [4.18-8.15]	1.94	11.08 [8.91 – 13.62]	7.1 [5.73 – 8.69]	1.56
15 to 19	28.18 [24.37-32.41]	19.92 [16.56-23.75]	1.41	15.46 [12.98 – 18.29]	3.45 [2.53 – 4.60]	4.48
20 to 24	44.72 [40.26-49.54]	30.66 [26.11-35.77]	1.46	37.05 [33.50 – 40.86]	9.87 [8.16 – 11.82]	3.75

Figure 53 Three year lagged mean all-cause mortality rate per 100,000 in England by Index of Multiple Deprivation Quintile 2001 – 2017 in 1 to 24 year olds (both sexes).

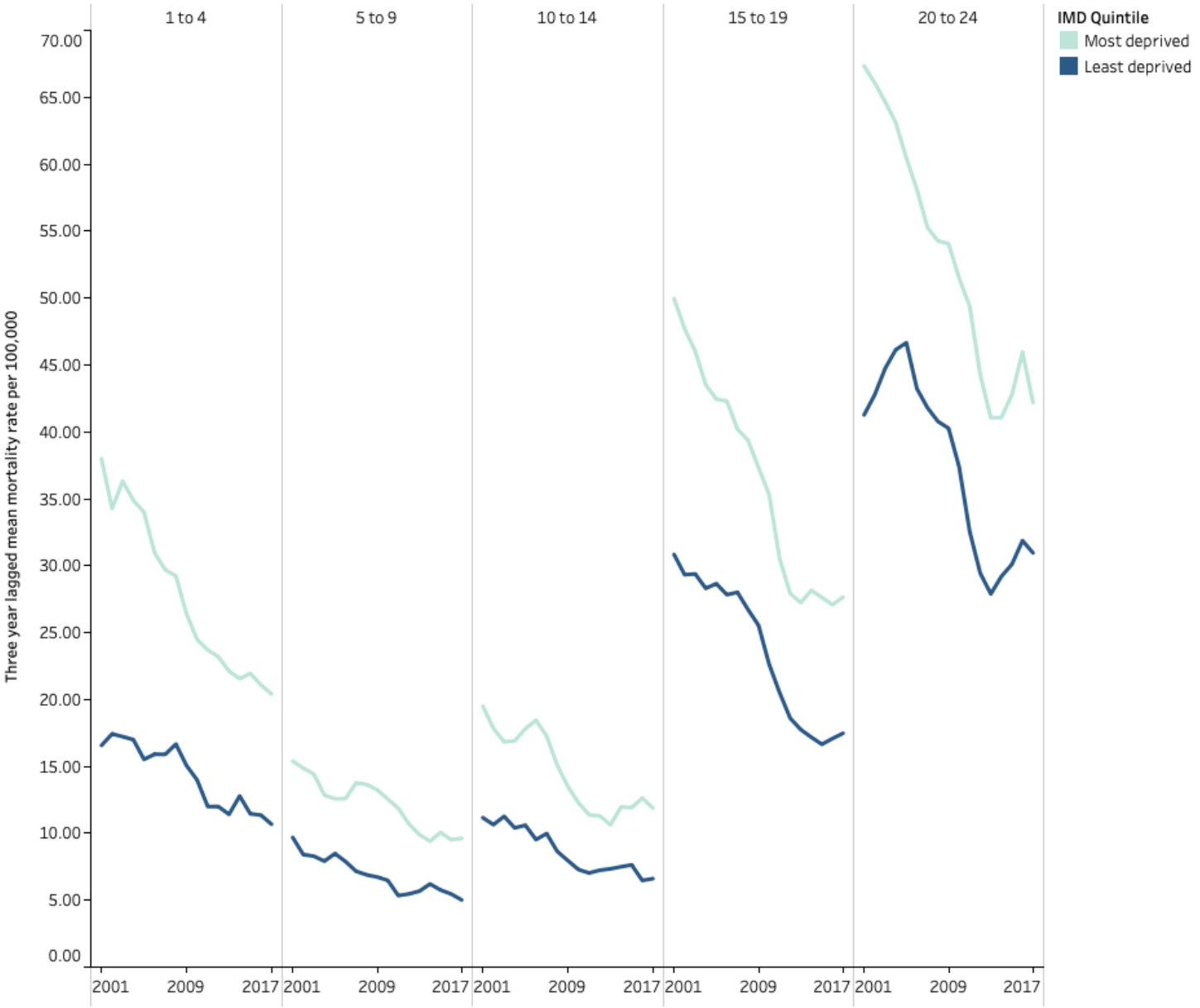
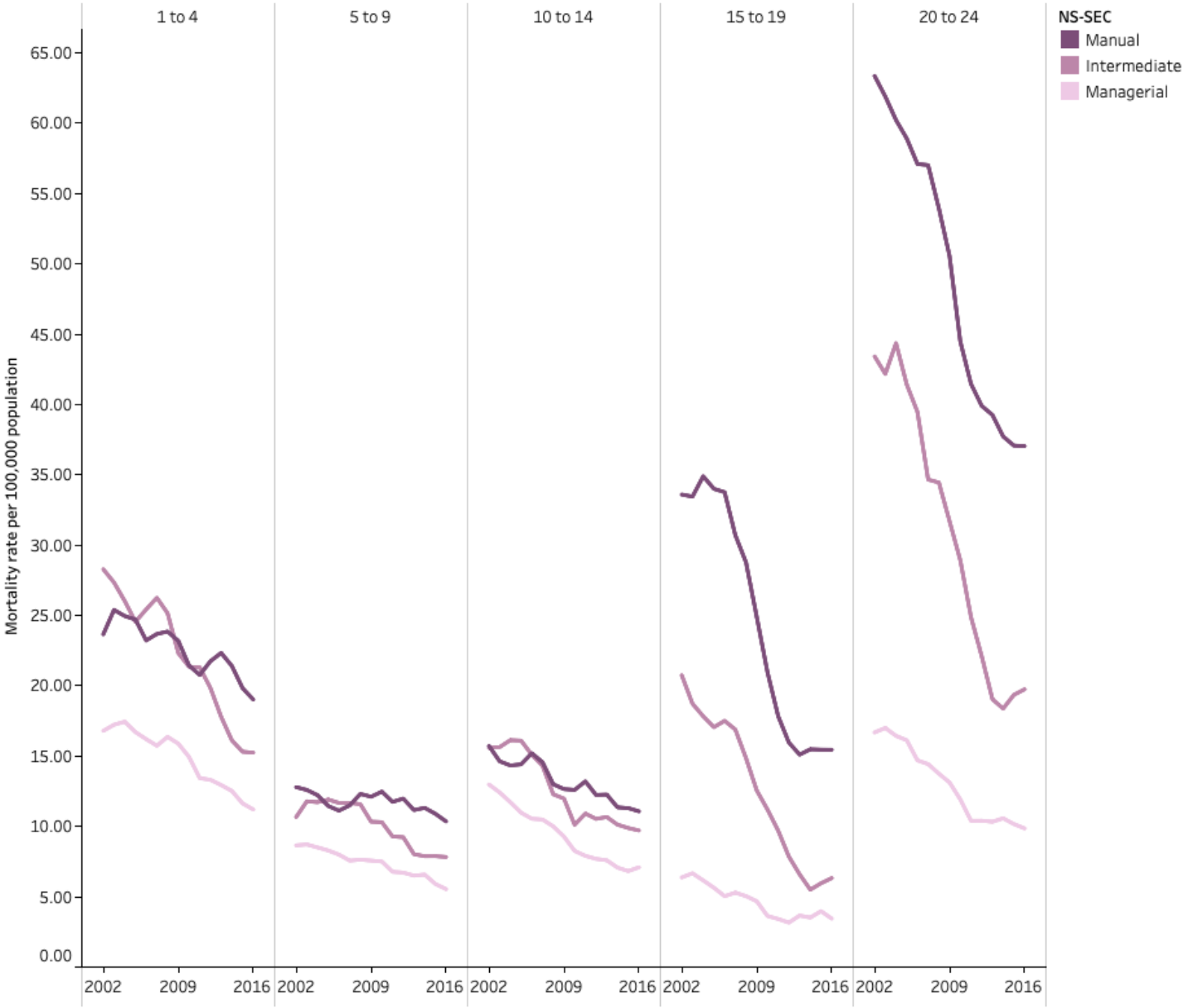


Figure 54 Three year lagged mean all-cause mortality rate per 100,000 in England by National Statistics Socioeconomic Classification 2002 – 2016 in 1 to 24 *year olds (both sexes).*



Local authority IMD score and child and young person mortality

Table 20 (p.189) shows the all-cause mortality rate in 2017 by age group and sex in the ten least and ten most deprived local authorities in England by IMD score. Cells are shaded green if the estimate is lower than England and uncertainty bounds do not overlap, and red if it is higher than England. In the 10 least deprived local authorities, most had all-cause mortality estimates which were significantly lower than England. However, among these local authorities the all-cause mortality rate was significantly higher than England in Richmond upon Thames, Rutland, Bracknell Forest, Kingston upon Thames and South Gloucestershire. There were also examples of local authorities with all-cause mortality rates which were lower than would be expected for their level of deprivation, particularly in 15-24 year olds in urban areas, for example in Hackney and Tower Hamlets (London), Birmingham, Liverpool, Manchester and Nottingham.

Linear regression models

Univariable analyses

Output from univariable models for the association between all-cause mortality (logged) by age group and sex and local authority IMD score, proportion of the local authority population BAME (logged), and proportion of the population aged 1-24, are shown in table 21 (p.190). Increased deprivation (higher local authority IMD) was associated with significantly higher all-cause mortality in all age and sex groups except 15-19 females and 20-24 in both sexes. Increased proportion of BAME within the local authority population was associated with significantly higher all-cause mortality in 1-4 females, 5-9 males, and significantly lower all-cause mortality in 15-19 and 20-24 males and females. Increased proportion of local authority population aged 1-24 was associated with significantly higher mortality in 1-4 males and females, and significantly lower mortality in 15-19 males and 20-24 males and females.

Multivariable analysis

Output from multivariable models are shown in tables 22 - 31 (p.191-200). After adjusting for other predictors in the final model, increasing deprivation (higher IMD) was associated with increased all-cause mortality (logged) in all age groups and both sexes except 5-9 and 10-14

females. Higher proportion of the population aged 1-24 was also found to be associated with significantly lower all-cause mortality amongst 5-9, 15-19 and 20-24 males, but not in females, after adjusting for proportion BAME, IMD score, and proportion aged 1-24. There were significant associations between local authority region and all-cause mortality in all age groups and both sexes, and the addition of region to models which included proportion aged 1-24, IMD score and proportion BAME was associated with improved model fit in all groups except 5-9 females.

Results from multi-level models were similar, and are shown in table 32 (p.201). The proportion of the variance which can be explained by geographic clustering of local authorities within regions increased with age, after adjusting for BAME proportion, IMD and proportion aged 1-24. Amongst 1-4, around 8-9% of the variance was explained by English region, compared with 17-18% in 15-19 year olds, and 23% and 42% in 20-24 males and females respectively

Table 20: All-cause mortality rate per 100,000[1] by age group and sex within the ten most and least deprived local authorities

10 least deprived local authorities

	1 to 4		5 to 9		10 to 14		15 to 19		20 to 24	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Wokingham	15.71 [11.36-21.37]	15.83 [11.85-20.66]	8.48 [7.47-9.53]	4.09 [3.54-4.71]	8.59 [7.89-9.38]	5.17 [4.66-5.70]	22.86 [20.27-25.72]	9.72 [8.75-10.95]	41.23 [36.60-46.53]	13.15 [11.72-14.96]
Windsor and Maidenhead	21.09 [15.27-28.60]	19.29 [14.44-24.98]	4.54 [4.00-5.10]	4.31 [3.73-4.96]	6.58 [6.01-7.17]	5.87 [5.28-6.46]	18.46 [16.47-20.61]	11.65 [10.36-12.97]	40.51 [36.17-45.37]	16.01 [14.12-17.99]
Surrey	9.10 [7.36-11.18]	9.36 [8.00-10.75]	6.41 [5.75-7.20]	3.56 [3.31-3.86]	4.69 [4.34-5.09]	5.97 [5.62-6.34]	23.53 [21.35-25.95]	11.10 [10.15-12.08]	48.51 [44.05-53.39]	18.32 [16.61-20.08]
Buckinghamshire	13.58 [10.62-16.94]	15.19 [11.64-19.23]	7.78 [6.61-9.10]	5.83 [5.05-6.72]	10.19 [9.25-11.29]	4.64 [4.22-5.05]	27.50 [24.84-30.27]	12.80 [11.61-14.02]	40.72 [36.70-44.80]	14.39 [12.89-15.95]
Richmond upon Thames	17.14 [12.88-22.67]	21.30 [15.21-28.49]	11.53 [10.51-12.64]	8.59 [8.01-9.23]	7.23 [6.72-7.75]	5.37 [5.01-5.76]	28.06 [25.31-31.08]	8.18 [7.31-9.04]	40.81 [36.76-45.14]	19.19 [16.98-21.39]
Rutland	24.06 [19.66-29.25]	5.58 [3.94-7.89]	5.34 [4.49-6.23]	1.51 [1.26-1.79]	7.06 [6.26-7.87]	4.64 [4.13-5.21]	25.56 [21.98-29.55]	13.43 [11.62-15.55]	51.19 [44.27-58.94]	15.11 [12.92-17.71]
West Berkshire	15.08 [13.06-17.41]	16.14 [11.64-21.52]	6.63 [5.79-7.53]	6.34 [5.54-7.19]	6.80 [6.21-7.45]	5.31 [4.81-5.83]	22.64 [20.29-25.37]	15.75 [13.96-17.58]	45.23 [40.61-50.68]	18.82 [16.48-21.27]
Bracknell Forest	15.52 [11.00-21.28]	15.76 [11.80-20.44]	9.78 [8.49-11.11]	3.08 [2.68-3.54]	9.87 [9.00-10.81]	4.71 [4.25-5.21]	21.67 [19.15-24.48]	10.00 [8.83-11.24]	42.38 [37.53-47.85]	13.66 [11.94-15.51]
Kingston upon Thames	21.23 [15.87-28.39]	17.60 [12.51-23.76]	7.75 [7.06-8.49]	5.28 [4.93-5.66]	3.90 [3.63-4.19]	7.20 [6.71-7.74]	22.59 [20.38-24.87]	23.17 [20.74-25.83]	38.82 [35.07-42.72]	15.79 [13.95-17.80]
South Gloucestershire	13.47 [9.97-17.23]	10.50 [7.58-13.89]	8.73 [7.88-9.70]	4.87 [4.47-5.32]	10.08 [9.35-10.82]	7.50 [6.96-8.04]	22.72 [20.39-25.38]	14.57 [13.08-16.13]	41.74 [37.54-46.68]	19.21 [17.11-21.45]

10 most deprived local authorities

	1 to 4		5 to 9		10 to 14		15 to 19		20 to 24	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Hackney	16.17 [14.01-18.55]	21.55 [18.84-24.25]	9.79 [8.91-10.74]	8.38 [7.86-8.92]	7.35 [6.86-7.85]	14.75 [13.86-15.69]	34.04 [30.80-37.38]	13.27 [12.03-14.63]	38.02 [34.43-41.82]	17.87 [16.03-19.87]
Tower Hamlets	15.67 [13.66-17.94]	19.37 [16.99-21.72]	12.48 [11.34-13.68]	5.55 [5.21-5.91]	10.56 [9.87-11.27]	7.69 [7.21-8.22]	23.25 [21.10-25.57]	12.64 [11.46-13.95]	33.72 [30.67-37.05]	17.86 [16.07-19.84]
Nottingham	19.14 [13.05-26.44]	20.22 [14.00-27.65]	7.52 [6.40-8.64]	2.30 [2.01-2.60]	9.33 [8.42-10.25]	10.48 [9.65-11.33]	21.71 [19.40-24.10]	17.49 [15.83-19.23]	28.58 [25.66-31.61]	15.96 [14.31-17.73]
Birmingham	24.47 [20.53-28.88]	18.21 [15.19-21.53]	11.39 [10.36-12.48]	7.09 [6.63-7.58]	10.91 [10.20-11.70]	6.46 [6.06-6.87]	23.53 [21.44-25.77]	16.59 [15.17-18.07]	37.28 [34.04-40.80]	29.47 [26.80-32.41]
Middlesbrough	20.64 [15.45-26.31]	18.17 [13.47-23.23]	13.61 [12.31-15.11]	5.22 [4.78-5.71]	10.70 [9.91-11.56]	6.45 [5.98-6.98]	18.40 [16.49-20.52]	17.47 [15.66-19.53]	55.78 [50.05-62.06]	20.45 [18.11-23.12]
Manchester	18.65 [14.92-22.99]	17.10 [13.89-20.74]	4.98 [4.41-5.62]	7.07 [6.33-7.86]	14.63 [13.49-15.84]	6.74 [6.25-7.27]	28.61 [25.90-31.34]	11.19 [10.22-12.20]	24.18 [21.97-26.46]	8.94 [8.08-9.83]
Kingston upon Hull, City of	19.79 [17.28-22.71]	17.11 [15.03-19.33]	9.45 [8.32-10.64]	10.08 [9.13-11.09]	10.20 [9.42-11.04]	10.36 [9.62-11.15]	41.05 [37.13-45.06]	21.42 [19.48-23.64]	75.60 [68.46-82.73]	20.71 [18.65-23.11]
Liverpool	19.54 [15.20-24.84]	15.94 [12.93-19.50]	9.06 [7.98-10.29]	9.02 [8.08-10.04]	12.64 [11.66-13.77]	7.13 [6.64-7.71]	35.53 [32.46-39.09]	19.84 [18.15-21.77]	38.09 [34.65-41.79]	16.83 [15.28-18.63]
Knowsley	18.41 [13.56-24.59]	30.97 [21.91-42.36]	12.04 [10.64-13.56]	9.87 [9.01-10.81]	13.30 [12.28-14.44]	16.85 [15.65-18.19]	36.48 [32.96-40.55]	31.44 [28.53-34.80]	53.24 [47.92-59.32]	15.37 [13.81-17.18]
Blackpool	26.42 [22.91-30.22]	29.93 [26.32-33.90]	5.98 [5.30-6.73]	3.54 [3.24-3.87]	6.87 [6.33-7.46]	5.79 [5.37-6.26]	39.12 [35.36-43.21]	25.27 [22.82-27.91]	73.79 [66.63-81.24]	21.65 [19.36-24.18]

Higher than England
Similar to England
Lower than England

[1]Cells are shaded green if the estimate is significantly lower than England, and red if the estimate is significantly higher than England.

Table 21: Coefficients (b) with 95% confidence intervals for univariable linear regression output for associations between local authority CYP all-cause mortality (logged) with IMD score, proportion of population BAME (logged) and proportion of population 1-24 by age group and sex in 2017

	IMD score				Proportion BAME				Proportion aged 1-24			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
1 to 4 Male	0.013	0.000	0.008	0.017	0.029	0.084	-0.004	0.063	1.891	0.002	0.704	3.078
1 to 4 Female	0.013	0.000	0.009	0.018	0.055	0.003	0.019	0.092	2.127	0.002	0.807	3.447
5 to 9 Male	0.009	0.020	0.002	0.017	0.062	0.036	0.004	0.119	0.211	0.845	-1.914	2.336
5 to 9 Female	0.013	0.008	0.003	0.023	0.024	0.509	-0.048	0.097	2.473	0.064	-0.146	5.092
10 to 14 Male	0.014	0.000	0.007	0.022	-0.041	0.153	-0.098	0.016	0.533	0.613	-1.547	2.613
10 to 14 Female	0.015	0.000	0.007	0.023	0.045	0.138	-0.015	0.104	1.934	0.077	-0.209	4.076
15 to 19 Male	0.011	0.000	0.005	0.017	-0.079	0.000	-0.121	-0.038	-2.080	0.009	-3.633	-0.526
15 to 19 Female	0.007	0.059	0.000	0.014	-0.118	0.000	-0.168	-0.068	-1.718	0.080	-3.644	0.207
20 to 24 Male	0.000	0.935	-0.006	0.005	-0.157	0.000	-0.190	-0.124	-4.612	0.000	-5.929	-3.295
20 to 24 Female	0.001	0.820	-0.006	0.008	-0.106	0.000	-0.153	-0.059	-2.950	0.001	-4.707	-1.192

Table 22: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority CYP all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 1 to 4 year old males in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.01	<0.001	0.01	0.02	0.01	<0.001	0.01	0.02	0.01	<0.001	0.01	0.02	0.01	<0.001	0.00	0.01
Proportion BAME (log)					0.01	0.48	-0.02	0.04	0.01	0.81	-0.03	0.04	0.04	0.17	-0.02	0.11
Proportion aged 1 to 24									0.39	0.63	-1.20	1.97	-0.01	0.99	-1.84	1.82
South East (baseline)																
East England													0.15	0.05	0.00	0.30
East Midlands													0.02	0.83	-0.15	0.19
London													-0.03	0.65	-0.18	0.11
North East													0.05	0.51	-0.11	0.22
Yorkshire & Humber													0.10	0.18	-0.05	0.25
North West													0.18	0.01	0.04	0.32
West Midlands													0.22	<0.001	0.07	0.37
South West													0.05	0.48	-0.09	0.19
Constant	2.58	<0.001	2.47	2.68	2.61	<0.001	2.47	2.75	2.49	<0.001	2.00	2.99	2.69	<0.001	2.06	3.32
R-squared	0.19				0.20				0.20				0.31			
AIC	-45.97				-44.48				-42.72				-49.66			
BIC	-39.96				-35.46				-30.70				-13.61			
					A vs B				B vs C				C vs D			
LRT					0.51				0.24				22.94			
LRT p value					0.48				0.62				0.00			

Table 23: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 1 to 4 year old females in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.01	0.00	0.01	0.02	0.01	0.00	0.01	0.02	0.01	0.00	0.01	0.02	0.01	0.01	0.00	0.01
Proportion BAME (log)					0.04	0.04	0.00	0.07	0.04	0.06	0.00	0.09	0.01	0.78	-0.06	0.08
Proportion aged 1 to 24									-0.38	0.67	-2.13	1.37	0.81	0.44	-1.23	2.85
South West (baseline)																
East England													0.10	0.26	-0.08	0.28
East Midlands													0.05	0.62	-0.15	0.24
North East													0.12	0.18	-0.06	0.30
West Midlands													0.16	0.07	-0.01	0.33
Yorkshire & Humber													0.20	0.02	0.04	0.36
London													0.22	0.02	0.04	0.41
North West													0.31	0.00	0.15	0.46
South East													0.09	0.25	-0.07	0.25
Constant	2.49	0.00	2.37	2.60	2.60	0.00	2.44	2.75	2.71	0.00	2.17	3.25	2.25	0.00	1.53	2.96
Observations	149.00				149.00				149.00				149.00			
R-squared	0.18				0.20				0.21				0.31			
AIC	-11.89				-14.29				-12.47				-17.19			
BIC	-5.88				-5.27				-0.46				18.85			
LRT					4.39				0.19				20.72			
LRT p value					0.04				0.66				0.01			

Table 24: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 5 to 9 year old males in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.01	0.02	0.00	0.02	0.01	0.05	0.00	0.02	0.01	0.00	0.00	0.02	0.02	0.00	0.01	0.03
Proportion BAME (log)					0.05	0.09	-0.01	0.11	0.11	0.00	0.04	0.18	0.07	0.27	-0.05	0.19
Proportion aged 1 to 24									-3.88	0.01	-6.79	-0.97	-3.65	0.04	-7.16	-0.13
North East (baseline)																
South West													0.27	0.09	-0.04	0.57
North West													0.14	0.31	-0.13	0.41
Yorkshire & Humber													0.21	0.17	-0.09	0.50
East England													0.47	0.01	0.12	0.81
East Midlands													0.34	0.06	-0.02	0.69
London													0.29	0.11	-0.07	0.64
West Midlands													0.28	0.09	-0.04	0.59
South East													0.22	0.17	-0.09	0.54
Constant	1.77	0.00	1.58	1.97	1.92	0.00	1.66	2.18	3.07	0.00	2.17	3.98	2.57	0.00	1.31	3.83
R-squared	0.04				0.06				0.10				0.15			
AIC	144.20				143.33				138.37				144.91			
BIC	150.20				152.34				150.39				180.96			
LRT					2.86				6.96				9.46			
LRT p value					0.09				0.01				0.30			

Table 25: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 5 to 9 year old females in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.01	0.01	0.00	0.02	0.01	0.01	0.00	0.02	0.01	0.05	0.00	0.02	0.00	0.99	-0.01	0.01
Proportion BAME (log)					0.00	0.90	-0.07	0.08	-0.02	0.65	-0.12	0.07	-0.04	0.57	-0.18	0.10
Proportion aged 1 to 24									1.66	0.38	-2.06	5.38	3.83	0.06	-0.23	7.89
East Midlands (baseline)																
East England													0.61	0.00	0.20	1.02
North East													0.57	0.01	0.16	0.98
South West													0.59	0.00	0.20	0.98
London													0.70	0.00	0.29	1.11
Yorkshire & Humber													0.96	0.00	0.58	1.35
West Midlands													1.00	0.00	0.61	1.39
North West													0.96	0.00	0.59	1.32
South East													0.51	0.01	0.14	0.88
Constant	1.39	0.00	1.15	1.63	1.40	0.00	1.08	1.73	0.91	0.12	-0.24	2.06	-0.21	0.78	-1.67	1.24
R-squared	0.05				0.05				0.05				0.27			
AIC	208.38				210.37				211.57				188.31			
BIC	214.39				219.38				223.59				224.36			
LRT					0.02				0.80				39.25			
LRT p value					0.90				0.37				0.00			

Table 26: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 10 to 14 year old males in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.01	0.00	0.01	0.02	0.02	0.00	0.01	0.02	0.02	0.00	0.01	0.02	0.01	0.02	0.00	0.02
Proportion BAME (log)					-0.07	0.02	-0.12	-0.01	-0.07	0.05	-0.14	0.00	0.07	0.23	-0.04	0.17
Proportion aged 1 to 24									0.33	0.82	-2.49	3.15	-1.80	0.26	-4.97	1.37
South East (baseline)																
East England													0.20	0.14	-0.07	0.46
Yorkshire & Humber													0.06	0.65	-0.20	0.31
South West													0.06	0.62	-0.18	0.31
East Midlands													0.08	0.60	-0.21	0.37
North East													0.20	0.17	-0.09	0.49
West Midlands													0.33	0.01	0.08	0.59
North West													0.31	0.01	0.07	0.55
London													-0.24	0.06	-0.50	0.01
Constant	1.92	0.00	1.73	2.10	1.73	0.00	1.48	1.97	1.63	0.00	0.75	2.50	2.60	0.00	1.50	3.69
R-squared	0.09				0.12				0.12				0.28			
AIC	130.39				126.90				128.85				114.39			
BIC	136.40				135.92				140.86				150.43			
LRT					5.48				0.06				30.46			
LRT p value					0.02				0.81				0.00			

Table 27: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 10 to 14 year old females in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.02	0.00	0.01	0.02	0.01	0.00	0.01	0.02	0.02	0.00	0.01	0.02	0.01	0.05	0.00	0.02
Proportion BAME (log)					0.02	0.44	-0.04	0.08	0.03	0.38	-0.04	0.11	-0.04	0.51	-0.15	0.07
Proportion aged 1 to 24									-0.66	0.66	-3.63	2.30	1.30	0.44	-2.03	4.63
East England (baseline)																
South West													0.22	0.14	-0.07	0.51
North East													0.04	0.79	-0.28	0.37
West Midlands													0.33	0.03	0.03	0.62
East Midlands													0.30	0.08	-0.04	0.63
North West													0.26	0.07	-0.02	0.54
London													0.44	0.00	0.16	0.72
Yorkshire & Humber													0.62	0.00	0.32	0.91
South East													0.09	0.53	-0.19	0.36
Constant	1.64	0.00	1.45	1.83	1.71	0.00	1.45	1.97	1.90	0.00	0.99	2.82	1.02	0.07	-0.10	2.15
R-squared	0.09				0.10				0.10				0.27			
AIC	140.86				142.26				144.06				128.67			
BIC	146.87				151.27				156.07				164.72			
LRT					0.60				0.20				31.39			
LRT p value					0.44				0.65				0.00			

Table 28: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 15 to 19 year old males in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.01	0.00	0.01	0.02	0.01	0.00	0.01	0.02	0.02	0.00	0.01	0.02	0.01	0.00	0.01	0.02
Proportion BAME (log)					-0.10	0.00	-0.14	-0.06	-0.06	0.03	-0.11	-0.01	0.00	0.91	-0.08	0.07
Proportion aged 1 to 24									-2.84	0.01	-4.81	-0.87	-3.77	0.00	-5.98	-1.57
East England (baseline)																
South West													0.02	0.83	-0.17	0.21
London													0.09	0.32	-0.09	0.28
West Midlands													0.15	0.12	-0.04	0.34
East Midlands													0.34	0.00	0.11	0.56
North East													0.26	0.02	0.04	0.47
North West													0.26	0.01	0.08	0.45
Yorkshire & Humber													0.43	0.00	0.23	0.62
South East													0.19	0.04	0.00	0.37
Constant	3.08	0.00	2.94	3.23	2.79	0.00	2.61	2.97	3.63	0.00	3.02	4.24	3.93	0.00	3.19	4.68
R-squared	0.09				0.22				0.26				0.40			
AIC	49.68				28.29				22.18				6.06			
BIC	55.69				37.30				34.20				42.11			
LRT					23.39				8.11				32.12			
LRT p value					0.00				0.00				0.00			

Table 29: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 15 to 19 year old females in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.01	0.06	0.00	0.01	0.01	0.00	0.00	0.02	0.01	0.01	0.00	0.02	0.01	0.02	0.00	0.02
Proportion BAME (log)					-0.13	0.00	-0.18	-0.08	-0.14	0.00	-0.20	-0.07	-0.03	0.50	-0.13	0.06
Proportion aged 1 to 24									0.23	0.86	-2.31	2.76	-1.50	0.29	-4.29	1.28
London (baseline)																
Yorkshire & Humber													0.16	0.20	-0.08	0.40
North East													0.15	0.30	-0.13	0.43
East Midlands													0.26	0.07	-0.02	0.54
West Midlands													0.40	0.00	0.18	0.62
East England													0.43	0.00	0.19	0.66
North West													0.46	0.00	0.23	0.69
South West													0.47	0.00	0.22	0.72
South East													0.16	0.17	-0.07	0.38
Constant	2.53	0.00	2.35	2.71	2.13	0.00	1.91	2.35	2.06	0.00	1.28	2.85	2.57	0.00	1.73	3.42
R-squared	0.02				0.18				0.18				0.37			
AIC	119.79				95.24				97.20				75.75			
BIC	125.80				104.25				109.22				111.80			
LRT					26.56				0.03				37.45			
LRT p value					0.00				0.86				0.00			

Table 30: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 20 to 24 year old males in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.00	0.94	-0.01	0.01	0.00	0.06	0.00	0.01	0.01	0.00	0.00	0.01	0.01	0.00	0.00	0.01
Proportion BAME (log)					-0.16	0.00	-0.20	-0.13	-0.12	0.00	-0.16	-0.08	-0.06	0.06	-0.12	0.00
Proportion aged 1 to 24									-2.73	0.00	-4.38	-1.09	-4.34	0.00	-6.12	-2.57
London (baseline)																
South East													0.14	0.05	0.00	0.29
North West													0.07	0.33	-0.07	0.22
South West													0.06	0.50	-0.11	0.22
East England													0.29	0.00	0.14	0.44
Yorkshire & Humber													0.34	0.00	0.19	0.50
East Midlands													0.32	0.00	0.14	0.50
North East													0.23	0.01	0.05	0.41
West Midlands													0.11	0.14	-0.03	0.25
Constant	3.90	0.00	3.76	4.04	3.42	0.00	3.27	3.57	4.23	0.00	3.72	4.74	4.69	0.00	4.15	5.23
R-squared	0.00				0.39				0.43				0.57			
AIC	49.14				-23.06				-31.77				-57.95			
BIC	55.15				-14.05				-19.75				-21.90			
LRT					74.20				10.71				42.18			
LRT p value					0.00				0.00				0.00			

Table 31: Coefficients (b) with 95% confidence intervals for multivariable linear regression output for associations between local authority level all-cause mortality (logged) with IMD, proportion of population BAME (logged), proportion of population 1-24 and English region in 20 to 24 year old females in 2017

	Model A				Model B				Model C				Model D			
	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper	b	p	lower	upper
IMD	0.00	0.82	-0.01	0.01	0.00	0.24	0.00	0.01	0.01	0.10	0.00	0.01	0.00	0.38	0.00	0.01
Proportion BAME (log)					-0.11	0.00	-0.16	-0.06	-0.09	0.01	-0.15	-0.02	-0.05	0.26	-0.12	0.03
Proportion aged 1 to 24									-1.69	0.17	-4.13	0.75	-1.82	0.12	-4.15	0.50
North East (baseline)																
South East													0.13	0.23	-0.08	0.34
London													0.16	0.18	-0.07	0.40
North West													0.41	0.00	0.23	0.59
East England													0.48	0.00	0.25	0.70
Yorkshire & Humber													0.56	0.00	0.36	0.75
South West													0.42	0.00	0.22	0.63
West Midlands													0.66	0.00	0.45	0.87
East Midlands													0.05	0.66	-0.18	0.29
Constant	2.99	0.00	2.82	3.16	2.66	0.00	2.45	2.87	3.16	0.00	2.41	3.92	3.05	0.00	2.22	3.88
R-squared	0.00				0.13				0.14				0.50			
AIC	103.81				85.62				85.70				21.89			
BIC	109.82				94.63				97.71				57.94			
LRT					20.19				1.92				79.81			
LRT p value					0.00				0.17				0.00			

Table 32: Coefficients (b) with 95% confidence intervals from mixed effects output for associations between local authority level all-cause mortality (logged), IMD, proportion of population BAME (logged), proportion of population 1-24 in 2017. Intra Class Coefficient (ICC) shows proportion of variance between local authorities explained by clustering within English regions.

	Males 1-4	Females 1-4	Males 5-9	Females 5-9	Males 10-14	Females 10-14	Males 15-19	Females 15-19	Males 20-24	Females 20-24
IMD										
b	0.01	0.01	0.01	0.00	0.01	0.01	0.01	0.01	0.01	0.00
P	<0.001	<0.001	<0.001	0.68	0.01	0.02	<0.001	0.01	<0.001	0.33
95% CI	0.01 - 0.02	0.00 - 0.02	0.00 - 0.02	-0.01 - 0.01	0.00 - 0.02	0.00 - 0.02	0.01 - 0.02	0.00 - 0.02	0.00 - 0.01	0.00 - 0.01
Prop BAME (log)										
b	0.03	0.03	0.11	-0.03	0.02	-0.02	-0.02	-0.06	-0.07	-0.04
P	0.26	0.31	<0.001	0.65	0.67	0.75	0.47	0.16	0.01	0.24
95% CI	-0.02 - 0.08	-0.03 - 0.08	0.04 - 0.18	-0.15 - 0.10	-0.07 - 0.11	-0.11 - 0.08	-0.09 - 0.04	-0.14 - 0.02	-0.13 - -0.02	-0.12 - 0.03
Proportion 1-24										
b	0.11	0.17	-3.88	3.18	-1.11	0.72	-3.43	-1.04	-3.95	-1.89
P	0.90	0.86	0.01	0.11	0.46	0.65	<0.001	0.43	<0.001	0.10
95% CI	-1.54 - 1.76	-1.66 - 1.99	-6.72 - -1.03	-0.67 - 7.02	-4.04 - 1.81	-2.36 - 3.81	-5.49 - -1.37	-3.64 - 1.56	-5.63 - -2.27	-4.13 - 0.35
Constant										
b	2.67	2.57	3.07	0.62	2.35	1.47	3.94	2.64	4.70	3.39
P	<0.001	<0.001	<0.001	0.35	<0.001	0.01	<0.001	<0.001	<0.001	<0.001
95% CI	2.13 - 3.21	1.98 - 3.17	2.19 - 3.96	-0.67 - 1.91	1.38 - 3.31	0.44 - 2.49	3.26 - 4.63	1.78 - 3.51	4.14 - 5.27	2.62 - 4.15
ICC	0.09	0.08	0.00	0.24	0.14	0.16	0.17	0.18	0.23	0.42
95% CI	0.02 - 0.33	0.01 - 0.33	0.00 - 0.00	0.08 - 0.53	0.04 - 0.39	0.05 - 0.42	0.05 - 0.45	0.06 - 0.44	0.08 - 0.50	0.20 - 0.68

Chapter 6 discussion

These results show steep gradients in CYP mortality by both area and individual level socioeconomic status, consistent with multiple studies of mortality in the UK and other high-income countries.[12,19,27-39] I found around a fifth of deaths in 1-24 may have been avoided if all IMD categories had the same mortality rate as the least deprived IMD category in 2018; over a ten year period this amounts to more than 7000 deaths. This is consistent with a recent analysis from The National Child Mortality Database of all 3227 deaths in 0-17 year olds in England in 2019.[45] In their report, the authors found around a quarter of deaths in 0-17 could be avoided if all areas of the country had CYP mortality rates comparable to the least deprived IMD quintile.[45]

I found the strength of social gradients in mortality to vary with age and sex, and how socioeconomic status was measured. Previous studies have also noted differences when using area or individual level metrics for socioeconomic status, although the evidence for this is mixed and mainly focuses on adults.[31,39] Using NS-SEC, I found variation in all-cause mortality between "manual" and "managerial" occupations was greatest in adolescents and young adults, but with large differences in 1-14 year olds also noted, and widening inequalities in 5-14 year olds since 2002. I also found wide variation in mortality by IMD quintile category, but in contrast to NS-SEC this was greatest in younger groups. However, the mortality rate for adolescents and young adults living in the most deprived areas of England was still around 40% higher than in the least deprived area in 2018.

Variation in associations between local authority deprivation, ethnicity, age structure and CYP mortality also differed by age group and sex. Univariable analyses showed associations between local authority deprivation score and all-cause mortality in both sexes in 1-4, 5-9 and 10-14, and males 15-19, with no significant associations found in females 15-19 and both sexes 20-24. Associations between CYP mortality and other local authority characteristics also differed by age group. Increasing proportion of local authority population who were from minority ethnic groups and aged 1-24 was associated with significantly higher mortality in 1-9 year olds and significantly lower mortality in 15-24 year olds. These contrasting patterns are reflected in multivariable models of associations between deprivation score and local

authority demographic factors. Amongst males, there were significant associations between deprivation and CYP mortality in all age groups after adjusting for demographic factors, whereas for females this was only this case in 1-4 and 15-19 females.

Previous work has suggested that socioeconomic gradients decrease during adolescence; i.e. that there is "equalisation" in health outcomes including mortality[36,224-226] and morbidity.[227-230] Although my results demonstrate social gradients in CYP mortality throughout adolescence, these associations were weakest in this age group when analysing mortality by IMD category. Explanations for this have included the increasing importance of peer relationships and opportunities for social mixing in schools, and increase in autonomy and risk taking, which may mediate the influence of family socioeconomic status on health outcomes.[224,228,231] However, other work examining these relationships have found strong social gradients during adolescence,[232,233] with some suggesting an exacerbation on inequalities during this period of the life-course.[234]

These inconsistencies may reflect the differing burden of specific causes of death by age group and sex shown in Chapter 3, but also the complex transitions which occur during adolescence. These include physical, cognitive, behavioural and emotional development, but also social development with the increase in importance of peer relationships outside the family.[235-237] It is likely that different mechanisms operate with regard to deprivation and health in young people, as their social environment transitions from that of children (embedded in families) to adulthood (living independently).[214] There are multiple important indicators for these, identified by the World Bank has those within education, work, family, citizenship and taking individual responsibility for health.[238] As a result, the importance of different determinants of health within Dahlgren and Whitehead's conceptual model[23] are likely to differ between younger and older CYP, both at the level of the individual, but also within families, schools and communities, to distal structural factors. These complexities highlight the need to analyse social gradients in health in adolescents separately from young children and adults, yet data required to do this are sparse.[214]

Analyses of social gradients in young people are further compounded by challenges in measuring socioeconomic status in this age group.[234] As young people move away from home

for employment or education the effect of area level deprivation is difficult to interpret, and how best to classify individual metrics for socioeconomic status in this age group is unclear. Due to concerns around data accuracy for both deaths and population denominators, I chose to exclude adolescents who were classified as students within analyses of mortality by NS-SEC, which may have both under or over-estimated social gradients in this age group

Consistent with previous work, I found much of the variation in CYP mortality by English region can be explained by levels of deprivation within local authorities. A study of variation in differences in health amongst adults within 8797 ward in England and Wales found differences to be attributed to SES more than to geographic region,[239] similar to Newton et al. in their analysis of variation in life expectancy by English Region.[212] However, I found this to vary with age in mixed-effects models, reflecting differences in the strength of social gradients in CYP mortality by age group described above. After adjusting for local authority deprivation score, population aged 1-24 and proportion from ethnic minorities, I found only around 8% of the variance in all-cause mortality between local authorities to be explained by clustering within English region in 1-4 year olds, but this rose to between 20-40% in 20-24 year olds. This suggests variation in the extent to which determinants of health are captured in these models by age group, and of the increasing importance of unmeasured determinants (potentially including health service factors) among adolescents compared with young children.

Strengths and weaknesses

Strengths of these analyses include the use of both individual and area level metrics for socioeconomic status, that I assess variation in the strength of associations by age group and sex, and analyse how geographic variation in CYP mortality can be explained by deprivation and demographic factors in different age groups. The key weakness of this analysis is that I did not examine differences in social gradients by cause, which have previously been described.[31,39,45,240] As described in Chapter 3, there is large variation in the burden of mortality burden by sex and age group in 1-24 year olds, particularly in older groups. Contrasting trends in associations by demographic and socioeconomic characteristics of local

authorities shown above likely reflect this, but are difficult to interpret using all-cause mortality alone.

Further limitations to this work include the use of modelled data provided by the GBD for examining local authority level CYP mortality and deprivation. These estimates are subject to the same limitations within the GBD estimation process as described in Chapter 5. I measured ethnic differences between local authorities as a binary exposure (White ethnicity compared with BAME), and did not account for variation between diverse ethnic minority populations and CYP mortality. I also excluded CYP within unemployed and full time students when assessing individual/family level variation in mortality using NS-SEC, which further complicates interpretations of these results in adolescents. Although I assessed for problematic collinearity in multivariable models, the estimates for variance inflation factors and scatter plots shown in figure 52 (p.181) demonstrate a degree of collinearity which may have affected my results. Finally, many of these analyses describe associations at the population level which may not be reflected at the individual level.

Mechanisms through which social factors are associated with child and young person mortality

In order to address social gradients in CYP mortality described here it is important to consider how they operate. Pearce et al. and others discuss the mechanisms through which socioeconomic status results in inequities in CYP health as being related to material, psychological, behavioural and structural factors.[24,241] As described above, the relative importance of these is likely to differ between adolescents and younger age groups.[214] In terms of material factors, CYP from more affluent families have greater access to resources to promote health.[241] Even in high-income countries such as the UK, poorer families may simply struggle to afford items that are essential to CYP health and survival, such as nutritious food and appropriate clothing for their children.[24,242] CYP from deprived backgrounds are also more likely to live in overcrowded and poor quality housing, (although the association between housing cost and quality is complex).[241] Factors relating to housing quality include the presence of condensation and damp, which may exacerbate existing health problems, and increased vulnerability to injury and accidents inside the home, including fire-related injuries.[57,58,243] Material pathways also include factors relating the built environment where

CYP live, with access to safe spaces to play, population density, and air pollution associated with household income.[244] Importantly, although the NHS provides highly equitable access to health services in the UK compared to many countries,[245] material deprivation can still result in barriers to accessing services. These may include those related to travel, reduced access to technology required to access some services, and indirect costs through loss of earnings or employment as a result of caring for CYP who are unwell or have complex needs.[246]

Psychological pathways to poor health include how social inequality may be associated with levels of stress, feelings of inferiority and lack of control. The evidence base for these factors is focused on adults and the effect of control within the workplace,[247] but these are also likely to affect CYP health via indirect effects on care givers.[24] For example, financial strain may have negative impacts on parental mental health, indirectly affecting perinatal outcomes and subsequent CYP mortality. There may be more direct effects amongst older adolescents and young adults, as perceived family wealth relative to peers has been shown to be associated with self-reported health and wellbeing amongst adolescents, after adjusting for other aspects of socioeconomic status.[248] There are multiple health behaviours which are also associated with deprivation and are likely to affect CYP health including mortality. These include parental cigarette smoking, alcohol and substance misuse. However, these individual health behaviours are heavily influenced by broader social factors which limit the capacity for care-givers to provide healthy environments for CYP.[26]

Structural social determinants of health refer to political, economic and cultural factors affecting the distribution of power, services and resources in a population.[24] This includes factors related to total wealth within societies, distribution of income, and investment in education, health and social care and welfare systems.[249-251] Although national income is an powerful determinant of CYP mortality, this association depreciates with increasing wealth, and is less important among high-income countries.[252] Further, societies with greater differences in income distribution have multiple worse health outcomes, including high-income countries such as the UK, after adjusting for national income.[253-256] Multiple mechanisms have been proposed to explain this association.[257] These include psychological factors which are similar to those described above; that poor individual health can be associated with perception of others both above and below oneself in the social and income

hierarchy. Large differences within this hierarchy create "status anxiety", leading to chronic stress and worse health outcomes for adult carers and consequently CYP.[251] Greater inequality is also thought to erode factors related to "social capital" within communities.[258,259] This may operate through increasing hostility, violence and discrimination, and reduced levels of trust and group membership,[260-262] which weaken social affiliations and exacerbates the impact of low social status on health.[261] There is evidence that income inequality may also exacerbating existing health inequalities and weaken a society's willingness to invest in improvements that promote wellbeing.[263-266] These have direct influences on CYP health, but also operate via the material, psychological and behavioural pathways described above. There are also periods of the life course which are particularly vulnerable to these factors; social disadvantage early in childhood can expose CYP to further risk, is associated with worse health outcomes in adolescence and later adulthood, and impacts health for the next generation.[26]

The UK's high levels of poverty, material deprivation, and income inequality are likely to be important contributors UK's poor mortality outcomes for CYP described in this thesis.[12,13,14,267] Being born into poverty increases the risk of multiple factors contributing to poor health across the life course,[267] and the UK has higher levels of child poverty than the best performing EU15+ countries for mortality,[268] with rates continuing to rise even prior to the COVID-19 pandemic.[269] Addressing socioeconomic factors associated with poor health is complex, but there are clear opportunities to do so. These need to be designed to incorporate the multiple pathways through which socioeconomic disadvantage affects health as described above, but also acknowledge differences in exposure to mortality risk, vulnerability, and the effects of ill health associated with deprivation. In the main discussion of this thesis, I will discuss how these relate to multiple determinants of health, including the role health systems may play in addressing inequities in mortality related to social factors.

Conclusions

The analyses presented in this chapter demonstrate steep social gradients in CYP mortality. However, the extent to which socioeconomic and demographic factors explain geographic variation in outcomes described in Chapter 5 varies by age group. Other health determinants

which may explain geographic variation, and resultant international differences in mortality, include health service factors. We will assess these by first describing patterns of emergency healthcare use in England in Chapter 7, and then identifying healthcare behaviours which are associated with increased mortality risk for CYP with chronic conditions where the UK has higher mortality than the EU15+ in Chapter 8.

Chapter 7

Hospital Episode Statistics and population level healthcare activity amongst children and young people in England

Previous chapters in this thesis have described how slow reductions in UK CYP mortality have resulted in current excess deaths compared with the EU15+, and that forecast mortality data suggest these differences are likely to widen. Cause specific analysis in Chapter 4 identified mortality due to neurological conditions (epilepsy), chronic respiratory conditions (asthma) and diabetes/endocrine conditions to be significantly higher in the UK than the EU15+. Understanding these differences requires exploring factors related to multiple determinants of health, perhaps the most important of which are socioeconomic factors. In Chapter 5 and 6 we have shown how individual or family socioeconomic status is strongly associated with CYP mortality, and that much of the geographic variation in mortality can be explained by deprivation. However, the strength of these associations varies with age, highlighting the need to explore other interlinked determinants of CYP mortality, including health service factors.

Equitable access to healthcare and professionals with appropriate training and equipment to manage childhood illnesses have been identified as important factors related to CYP mortality in high-income countries like the UK.[25] Deaths which should not occur with timely and effective medical care are referred to as *amenable*, and UK mortality rates for these conditions in 1-14 year olds are higher than many high-income countries.[270] Notably, although lists used to define amenable mortality are focused on adults, they include conditions where the UK has poor outcomes for CYP.[271] The Confidential Enquiry into Child and Maternal Health (CEMACH) also identified health service factors as contributing to CYP mortality[44], and recent analyses published by the National Child Mortality Database highlighted their importance to socioeconomic inequities in deaths.[45] Further, health service factors have been repeatedly recognised as contributing to deaths following individual case reviews.[80,272,273]

Examining patterns of health service activity in the UK may provide insights in to the contribution of health service factors to CYP mortality. Exploring activity within primary care will be essential to this, particularly with regard to the effectiveness of measures to prevent CYP requiring hospital admission. However, describing trends in secondary care activity by cause, age group and sex, will also provide insights as to changing demands placed on paediatric services, and inform requirements to adapt training and the structure of service provision. Identifying patterns of healthcare activity which are associated with death may provide further insights, including opportunities to identify individuals with high mortality risk in need of additional support.

In this chapter I will describe population level trends in emergency healthcare activity in CYP using Hospital Episode Statistics (HES) data. I will describe trends by age group, sex, region of England, Index of Multiple Deprivation (IMD), and admission cause. I will then focus on admission trends for chronic conditions where UK CYP mortality is higher than the EU15+: epilepsy, asthma and diabetes. This will provide context for further analyses of the contribution of health service factors and CYP mortality in Chapter 8, where I will examine individual level associations between patterns of healthcare activity and mortality hazard.

Aggregated HES data used here to describe the overall burden and trends of healthcare utilization in England amongst CYP also contributed to *Paediatrics 2040*, a project led by the Royal College of Paediatrics and Child Health (RCPCH) launched in Feb 2021.[274] *Paediatrics 2040* aimed to describe likely future changes needed to paediatric services in the UK. A key strand of this work was to understand how patterns and trends in health service utilization may be contributing to the UK's poor international performance for multiple health outcomes, including CYP mortality. The methods described here to clean HES data and classify cause of admission were discussed within the *Paediatrics 2040* Data and Evidence sub Committee, of which I am a member. Amendments referring to the NHS Digital Data Sharing Agreement to include use of the data for *Paediatrics 2040* were approved on 18th August 2020 (ref: NIC-141410), and Brent NHS Research Ethics Committee were updated regarding this on 30th July 2020. I would also like to specifically acknowledge the input of Eilis Keeble and Dougal Hargreaves at the Nuffield Trust who provided support and advice in developing these methods.

Related publication (under review):

Ward J, Hargreaves D, Rogers M, Firth A, Turner S, Viner R. Recent and forecast post-COVID trends in hospital activity in England amongst 0 to 24 year olds: analyses using routine hospital administrative data. *medRxiv* 2021: 2021.02.11.21251584.

Chapter 7 methods

In this chapter I used Hospital Episodes Statistics (HES) data to describe trends in healthcare activity among CYP in England. Further details on this data source are provided in Chapter 2, including data structure, NHS Digital cleaning procedures, and data permissions. The analysis here is limited to emergency admission data provided within the Admitted Patient Care (APC) HES dataset.

Admitted patient care data preparation

The full APC data extract I used in this analysis consisted of 38,436,393 Finished Consultant Episodes (FCE) across 12 years between 2007/08 to 2018/19. Here I describe procedures to clean these data and prepare for analysis.

Finished consultant episodes which were removed

I removed 3,163,292 FCEs from the data as the usual place of residence was outside England, and so less likely to capture all hospital contacts. 199 FCEs were removed as the discharge date was recorded as occurring before admission date, and a further 426,665 FCEs were removed as they were duplicates in terms of the admission date, discharge date, episode start date, episode end date, provider code (i.e. NHS trust), admission method and discharge destination. A further 2,563,853 FCEs were removed from the financial year 2018 / 2019, as only provisional estimates were available for this year. Finally, 5,303 observations were removed as sex was not recorded or was unspecified.

Combining episodes of care

I then undertook the following procedures to populate start and end dates for FCEs, and merge observations which likely represented a single episode of care. Where the FCE start date was missing and the episode was the first in an Inpatient Spell (IPS), the IPS admission start date was used. Where the FCE start date was missing and the FCE was not the first in the IPS, the previous FCE end date within an IPS was used where available. FCE end dates were replaced with the IPS discharge date where this was the last FCE within an IPS (i.e. spellend == "Y"). Where the IPS discharge date was missing, this was replaced by any discharge date within the IPS where available. Where a patient was admitted twice on the same day, this was recorded as one admission with the discharge date taken as the longest amount of time from either admission. After these procedures there remained 32,277,081 FCEs available for analysis

Defining admission type

Similar to methods used by the Nuffield Trust,[168] I defined admission type using the first episode within an IPS. I defined FCEs as Emergency Admissions if the episode type was General, the patient classification was Ordinary Admission and the admission method was either: Accident and Emergency, General Practitioner, Bed Bureau, Consultant Clinic, Admission via Mental Health Crisis Resolution Team, Accident and Emergency Department of another provider where the patient has not been admitted, or Other Emergency Admission. I defined FCEs as Elective Admissions if the episode type was "General", the patient classification was "Ordinary Admission", and the decision to admit could be separated in time from the actual admission. These included admissions from a waiting list, booked admissions, and planned admissions. I defined FCEs as day cases if the if the patient classification was Day case admission, and the admission method was one of the elective admissions listed above. I defined FCEs as Maternity admissions if the patient classification was "Ordinary Admission" and the admission method was defined as either: Admitted ante-partum, Admitted post-partum, The birth of a baby in this health Care Provider, or Baby Born outside the healthcare provider except when born at home as intended. For maternity admissions, the FCE could be any episode type. All other FCEs were defined as either Transfers or "other".

Out of 32,277,081 FCEs, there were 30,341,429 separate admissions. Of these 11,177,805 (36.8%) were emergency admissions, 8,048,518 (26.5%) were maternity admissions, 6,732,596 (22.2%) were day case admissions, 2,294,197 (7.6%) were elective admissions and 2,088,313 (6.9%) were admissions following transfers or other sources. These proportions were crosschecked with analyses completed by the Nuffield Trust for CYP admissions in 2015/16, and were comparable.[168]

Defining cause of admission

Within the entire APC data extract there were 11,578 different ICD10 codes used to define primary cause for admission. In order to generate meaningful groups within this list, I first used the Global Burden of Disease (GBD) 2017 cause of death hierarchy to map admissions to one of 117 level 3 GBD cause groups. This successfully mapped only 4977 (43%) of causes of admission codes, with the remaining mapped as "garbage codes." I then used the GBD2017 non-fatal cause hierarchy, to map 3,498 ICD10 codes to a further 23 GBD cause groups. On review of the remaining ICD10 codes, I was able to map a further 721 to GBD fatal or non-fatal cause groups, taking a lower threshold to define admission than is used to determine cause of death or morbidity in the GBD.

A high proportion of the remaining primary diagnoses were still defined as "garbage codes" using the GBD definition. However, these do provide more meaningful information regarding reason for admission than when used in the context of classifying causes of mortality and morbidity. For example, it can be entirely appropriate to define reason for admission on the basis of a collection of symptoms or complaints, where a diagnosis has not yet been formalised, and these still provide useful insights in to trends in hospital activity. I mapped the remaining 2,382 ICD10 codes to 22 causes I defined myself, using a combination of ICD10 chapter heading and subchapter description. This allowed for the full spectrum of reasons for admission within diagnoses and symptoms and signs to be classified. These cause groups were reviewed within the *Paediatrics 2040* Data and Evidence Committee, which these analyses contributed to.

In the vast majority of cases where an external ICD10 code was used to define admission, the mechanism of injury was not included. As a result, is was not possible to use the GBD level 3 injury groups to distinguish between, for example, accidental injury, self-harm, or transport injuries. In place of this, all ICD-10 codes within either chapter 21 (Injury, poisoning and certain other consequences of external causes) or chapter 22 (External causes of mortality or morbidity) were defined as either "Injury", "Poisonings" or "Foreign body".

The full list of ICD-10 codes, 165 cause groups, and their description, and mapping method used, is available in supplementary material 4 online via: https://drive.google.com/file/d/1qoWJQUJ2IfWofKrHYWhOQEq9A-HY1aJo/view?usp=sharing

Population denominators

I used population denominators provided by ONS (www.ons.gov.uk) to calculate emergency admission rates per 100,000 population by age group, sex and cause. I also categorised attendance by region based upon usual place of residence (North East, North West, West Midlands, East Midlands, East of England, Greater London, South East, South West) and Index of Multiple Deprivation (IMD) quintile category from 1 (most deprived) to 5 (least deprived) also based on usual place of residence. I used IMD 2007 data for healthcare activity between 2007-2009, IMD 2010 for activity from 2010 – 2014 and IMD 2015 for all other activity.

Chapter 7 results

Emergency admissions in 2017

Emergency admission rates per 100,000 population for all-causes, and due to epilepsy, asthma and diabetes by age group, sex, and IMD quintile category in 2017 and percentage change since 2007 are shown in supplementary material 2.

In 2017, there were 2,034,776 admissions amongst 1-24 year olds in England, of which 916,069 (45.0%) were emergency admissions, 632,568 (31.1%) were day cases, 223,738 (11.0%) were maternity admissions, 166,309 (8.2%) were elective admissions and 96,092 (4.7%) were transfers or other types of admission.

Among emergency admissions, 47.8% were in males, with this proportion decreasing with age (57.2% in 1-4 compared with 36.2% in 20-24). Most emergency admissions were amongst 1-4 (30.2%), followed by 20-24 (24.2%), 15-19 (18.1%), 5-9 (14.7%) and 10-14 (12.9%). In 2017, the rate of emergency admissions in 1-24 in England was 57.1 per 1,000 population, and ranged from 46.2 in London to 73.6 in the North West. The rate of emergency admissions per 1,000 was lowest in females 5-9 (34.1) and highest in males 1-4 (112.9). The rate of emergency admission increased with increasing deprivation, ranging from 46.8 amongst CYP in the IMD quintile category 5 (least deprived) to 69.6 in IMD quintile category 1 (most deprived).

Emergency admissions 2007 – 2017

The annual number of emergency admissions in England increased by 23.1% between 2007 and 2017. The increase in total admissions was greater in females than males (27.6% compared with 18.5%). Relative change in the number of emergency admissions was greater in females than males in all age groups except 1-4, (40.3% increase in males compared with 38.9% in females). Amongst adolescents and young people (10-24), change in the number of emergency admissions was at least 20 percentage points higher in females than males in all age groups (10-14, 15-19 and 20-24). The number of emergency admissions has increased in all age groups except 15-19 year olds males (9.3% decline) and was greatest in 5-9 year old females (52.0% increase). There was also wide variation in relative change in number of

emergency admissions between regions of England, ranging from an increase of 41.6% in East of England to 4.9% in the North East.

The rate of emergency admissions in 1-24 year olds increased by 17.1% between 2007 and 2017. Increases in the rate of emergency admission over this period ranged from 33.4% in East of England to 4.0% in Yorkshire and Humber. Admission rates increased in all age groups except 15-19 and 20-24 males, (3.8 and 3.3% declines respectively), and were greatest in 5-9 females (27.8% increase).

Emergency admissions by cause

In 2017, injuries were the most common cause of admission in 1-24 for both sexes combined, (13.5% of the total). Three of the other top 5 causes in 1- 24 were due to infections: other unspecified infections (9.5%), upper respiratory infections (8.9%) and lower respiratory tract infections (5.0%). The last cause in the top five was non-specific abdominal or pelvic pain (6.2%).

Amongst 1-4, the leading level 3 causes of emergency admission were respiratory infections, diarrhoeal illnesses, other infections and injuries. Amongst 5 to 9, the leading cause of admission were injuries, followed by respiratory and other infections, asthma, and abdominal pain. Amongst 10-14 and 15-19, the leading causes were injuries, abdominal pain, psychiatric disorders, urinary diseases and poisoning. Amongst 20-24 the leading cause for admission was still injuries, with maternal disorders second, followed by abdominal pain, poisonings and urinary diseases.

Emergency admissions by cause 2007 – 2017

Change in emergency admission rates per 100,000 population by cause in 1-24 year olds is shown in figure 55 (p.218).

Amongst 1-4 year olds, there has been a large increase in admission rates due to infectious causes including respiratory illnesses, emerging as the leading cause of admission in this age

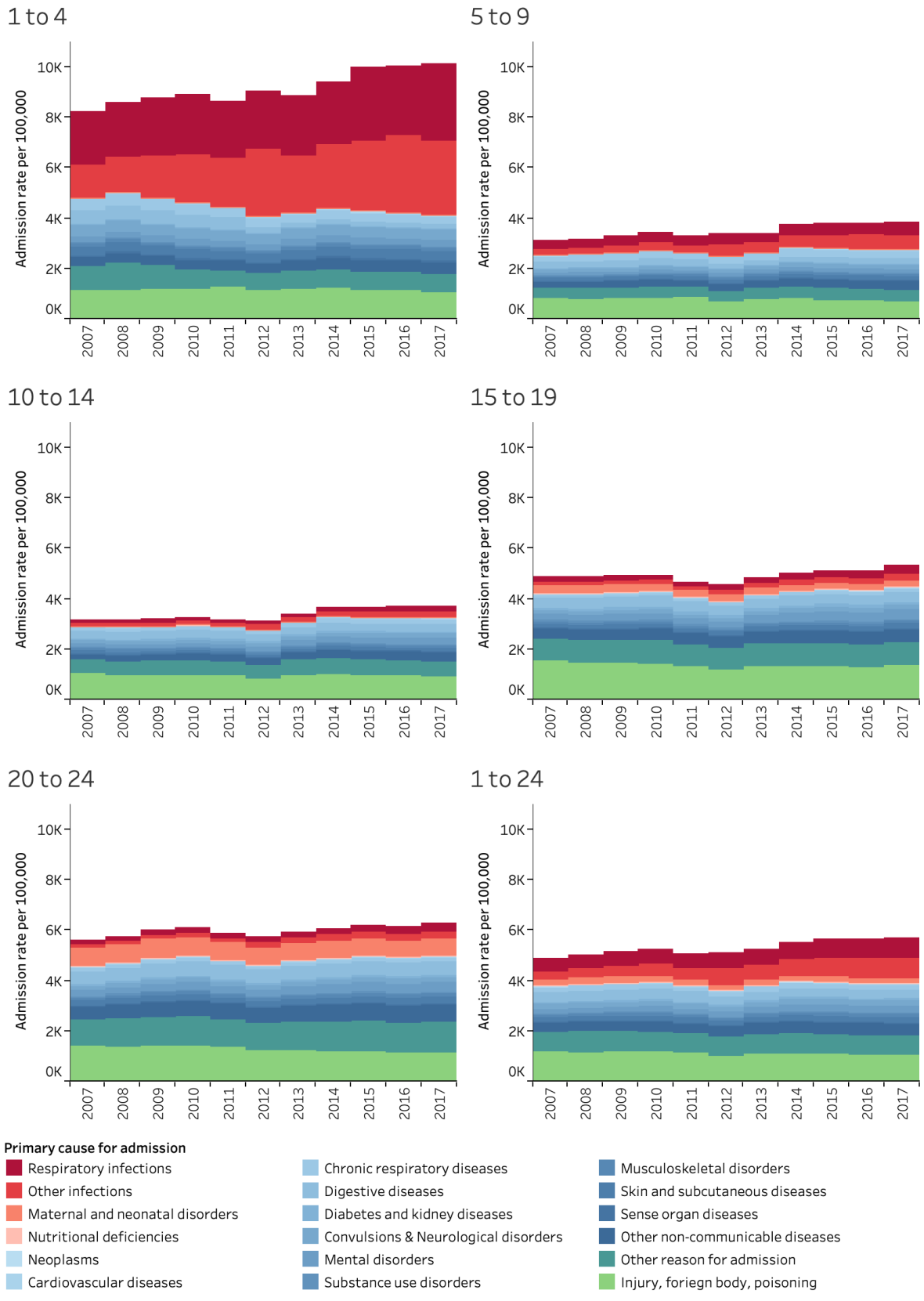
group from around 2011. Admission rates for most other causes have remained fairly stable over this time.

Amongst 5–9 there have been large increases in admission rates due to similar causes including respiratory and other infections, but also increases in admission rates for non-communicable diseases including chronic respiratory conditions and digestive disorders. Although admission rates due to injuries have remained fairly stable, they are still more than twice as high as any other cause and contribute to around 18% of the total burden in this age group.

Amongst the leading causes of admission in 10-14 year olds, there has been a sharp decline of around 18% between 2007 – 2017 in admissions due to injuries, although these still account for almost 20% of total admissions. Admissions due to mental disorders have increased sharply over this period, more than doubling and are now the third highest cause of admission in this age group.

Similar patterns are seen in 15-19 and 20-24, with sharp declines in admissions due to injuries (28 and 24% reduction respectively) and increases in admissions due to some mental disorders and urinary conditions. The other main causes for admission in this age group (poisonings and abdominal pain) have remained fairly stable.

Figure 55: Emergency admissions per 100,000 in England between 2007 – 2017 by cause and age group (1-24) both sexes



Patterns of emergency admissions with epilepsy in England

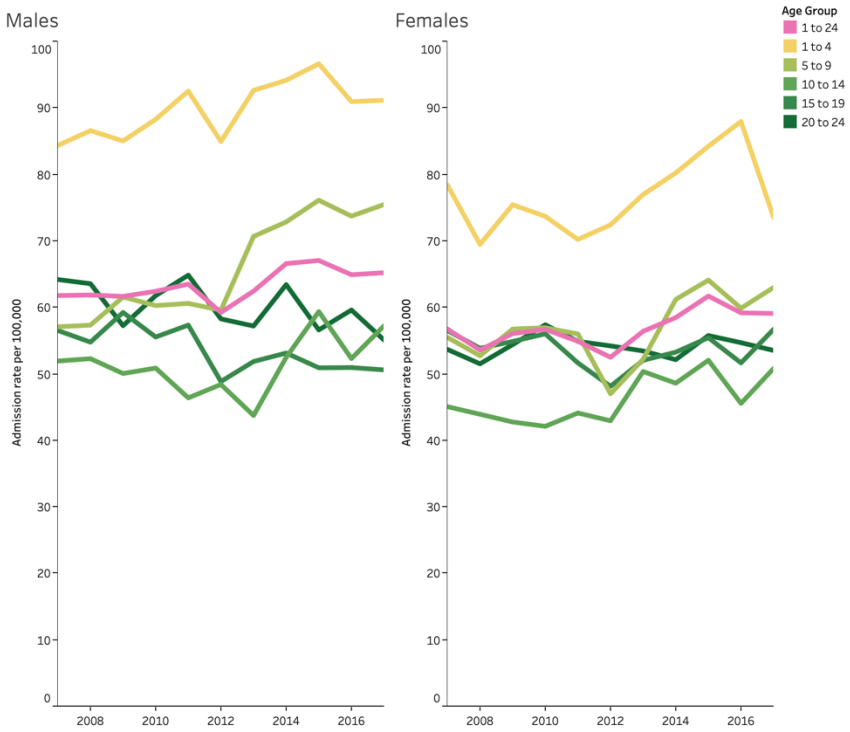
There were 9,988 emergency admissions amongst 1-24 year olds due to epilepsy in 2017 (1.1% of all admissions). 53.7% of these were amongst males, with this proportion decreasing with age (56.6% in 1-14 compared to 52.1% in 20-24). 24.3% of admissions were amongst 5-9, 22.6% amongst 1 to 4, 19.2% amongst 20-24, 17.2% amongst 10-14 and 16.8% amongst 15-19. The number of emergency admissions with epilepsy was associated with increasing level of deprivation; 30.3% of admissions were amongst CYP from the most deprived IMD quintile category, compared with 13.6% from the least deprived IMD quintile category. The number of emergency admissions with epilepsy ranged from 1625 in the South East (16.3%) to 520 in the North East (5.2%).

In 1-24 year olds, there were 62.3 [61.1 - 63.5] admissions per 100,000 population due to epilepsy in England in 2017, ranging from 51.9 [48.1 - 55.8] in East Midlands to 69.7 [63.9 - 76.0] in the North East. Admission rate was highest amongst CYP in the most deprived IMD quintile category (78.9) and lowest in the least deprived (47.7). The admission rate was highest amongst 1 to 4 (82.6) and lowest amongst 15-19 (53.6). The admission rate was higher amongst males than females 1-24 (65.2 compared with 59.1) and higher amongst males than females in all other age groups except 15-19.

Figure 56 (p.220) shows the emergency admission rate for epilepsy in England by age group between 2007 – 2017. The number of admissions in 1-24 due to epilepsy increased by 10.3% between 2007 and 2017 (11.7% increase amongst males and 8.6% amongst females), but has remained stable as a proportion of total admissions (around 1.2%). Most of the increase in number of admissions was driven by younger age groups, with the greatest relative change seen in 5-9 (57.6% increase amongst males and 35.0% amongst females), with 1-4 and 10-14 also seeing large increases in both sexes. Over the same period, the number of admissions for epilepsy amongst 15-19 decreased by 15.6% amongst males and 6.7% amongst females and amongst 20-24 they decreased amongst males by 9.4% and amongst females remained the same.

The admission rate due to epilepsy amongst 1-24 in England increased by 4.9% between 2007 and 2017. Admission rates increased in all ages except 15-19 and 20-24, where there were declines of 5.2 and 7.8% respectively. The largest increase in admission rates was in 5-9 (23.2% increase), with 10-14 increasing by 11.3% and rates in 1-4 remaining stable.

Figure 56: Emergency admission rate per 1,000 due to epilepsy by age group and sex in England 2007 - 2017



Patterns of emergency admissions with asthma in England

In 2017 there were 26,667 emergency admissions due to asthma in 1-24 in England. Overall, 54.3% emergency admission in 1-24 were amongst males, with large differences by age group: 64.8% of admission in 1-4 were amongst males, compared with 30.0% amongst 20-24. 33.3% of admissions were amongst 5-9, 24% were amongst 1-4, 18.3% were amongst 10-14, 13.0% were amongst 20-24 and 11.4% were amongst 15 to 19. 35% of admissions were amongst the most deprived IMD quintile category, compared with 11.3% in the least deprived quintile category.

In 2017 in England the emergency admission rate due to asthma was 166.2 per 1,000 population in England, ranging from 125.9 in East Midlands to 243.2 in North West. The admission rate for asthma amongst 1-24 was more than double amongst CYP from the most deprived IMD quintile category compared with the least deprived (248.8 compared with 105.6). The admission rate ranged from 254.2 per 1000 in 5-9 to 97.6 in 15-19. Sex differences in admission rates also varied by age group, with males aged 1-14 more likely to be admitted than females, with this trend reversing amongst 15-24.

The number of emergency admissions due to asthma amongst 1-24 increased by 2.0% between 2007 and 2017, but have declined as a proportion of total admissions from 3.5% in 2007 to 2.9% in 2017. The greatest increase in number of admissions was amongst 5-9, where admissions increased by 37.2%, resulting in this age group surpassing 1-4 as having the highest number of admissions by age group from 2015 onwards. The number of admissions declined in 1-4 by 39.9%, but increased in all other age groups; by 34.0% in 10-14, 19.8% in 15-19, and 21.9% in 20-24.

Figure 57 (p.223) shows the emergency admission rate for asthma in England by age group between 2007 – 2017. The admission rate due to asthma in 1-24 has declined by 2.9% between 2007 – 2017, driven by sharp declines in 1-4 which have almost halved (47.0% decrease). Admission rates in all other age groups have increased from between 34.2% in 10-14, 28.2% in 15-19, 19.0% in 20-24, and 15.3% in 5-9.

Patterns of emergency admissions with diabetes in England

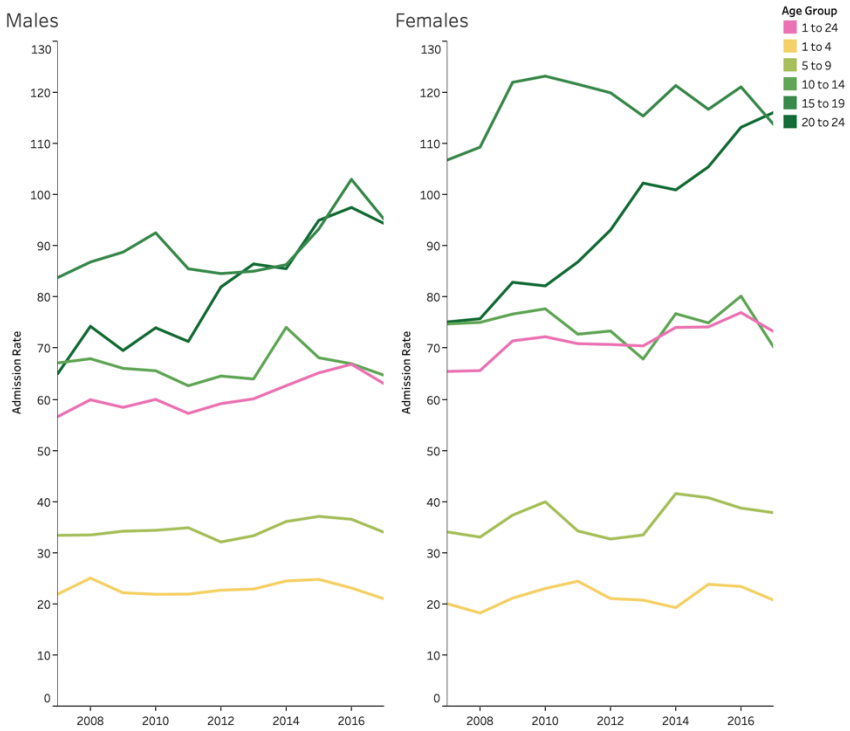
In 2017 there were 10,923 admissions with diabetes mellitus amongst 1-24 (1.2% of total admissions). 46.3% of admissions were amongst males, with this proportion varying little by age group. 33.9% of admissions were amongst 20-24, 29.8% amongst 15-19, 19.6% amongst 10-14, 11.5% amongst 5-9 and 5.2% amongst 1-4. There were 68.1 [66.8 – 69.4] admissions per 100,000 population in England due to diabetes in 2017, which ranged from 56.8 [53.9 – 59.7] in London to 83.1 [76.7 – 90.0] in the North East.

Figure 58 (p.223) shows the emergency admission rate for diabetes in England by age group between 2007 – 2017. The admission rate amongst 1-24 increased by 11.6% between 2007

and 2017, (11.3% increase amongst males and 11.9% increase amongst males). Amongst adolescents 10-24 (comprising more than 80% of all admissions), the largest increases have been in 20-24, where rates have increased by 20.0% over this period, and are now equivalent to those in 15-19 in both males and females.

Figure 57: Emergency admission rate per 1,000 due to asthma by age group and sex in England 2007 - 2017

Figure 58: Emergency admission rate per 1,000 due to diabetes mellitus by age group and sex in England 2007 - 2017



Chapter 7 discussion

In this chapter I describe trends in emergency admissions by age group and sex for CYP between 2007 - 2017, and for epilepsy, asthma and diabetes; chronic conditions which I have identified as having higher CYP mortality in the UK than the EU15+.

Consistent with previous work,[77,168] my findings show large increases in acute health service use amongst CYP over the last decade, but with variation by cause of admission, age group and sex. The majority of emergency admissions occur in 1-4 or 15-24 year olds, and there are steep social gradients for all causes examined. Geographic variation in admission rates is also stark, with the North West of England having almost double the emergency admission rates in London for 1-24 year olds. Infectious causes dominate admissions in younger age groups, with injuries and abdominal pain leading causes in 5-24.

I found contrasting trends in hospital activity for causes where the UK has high CYP mortality. Within diabetes and epilepsy there has been a steady increase in emergency admission rates, however with considerable year on year variation for epilepsy. Admissions due to asthma have followed a different pattern, with steep declines in admission amongst 1-4 contrasting with static or rising trends in other age groups. There are multiple potential explanations for these trends which will vary between causes, but the extent to which a proportion of these admissions may be avoidable warrants further study.

Drivers of healthcare activity include population growth, increasing expectations of medical care and changes in health-seeking behaviour, but also factors within the health service. Health service factors which are associated with unplanned emergency attendances include those related to primary care capacity and lack of preventative interventions in the community.[275] Previous work has shown that CYP who are registered with general practitioners in England who are more accessible have been found to be less likely to attend accident & emergency.[276,277] Sharp increases in emergency admissions for many causes may also reflect the fragmentation of services and poor integration of community and hospital based care. The NHS Long term plan has recognised this, and highlights improvements in

integration across primary and secondary care should be a focus to reduce pressure on emergency services.[21]

Integrated care models seek to coordinate services within and across healthcare and non-healthcare settings to better address health need. Improvements in integration may be effective in addressing increases in emergency hospital activity for CYP described in this analysis. The World Health Organization (WHO) defines the principles of integrated care as "Health services organized and managed so that people get the care they need, when they need it, in ways that are user friendly, achieve the desired results, and provide value for money."[278] Wolfe et al. used this to characterise integrated care models into four domains relating to the health needs of CYP.[66] Horizontal integration relates to how health, education and social care sectors interact and contribute to a holistic understanding of the needs of CYP. Poor horizontal integration is reflected in concern regarding communication across sectors with child health responsibilities, which has repeatedly been implicated in deaths in CYP, particularly where abuse is suspected but also for chronic conditions such as asthma.[272] Vertical integration describes co-ordination between primary and secondary care, for example primary care physicians working with specialists and mental health professionals. Longitudinal integration describes how health systems function at periods of change across the life course, for example when CYP transition from paediatric to adult services.[279] Finally, population based integration describes co-ordination between healthcare and public health, health promotion and disease prevention.[66]

Although it is reasonable to propose that improving integration across these domains will be beneficial to CYP health, the evidence base for this is limited. Much of integrated care research and policy has focused on the health and social care needs of the elderly, with relatively few studies investigating these models in CYP. Further, there are substantial challenges in assessing the effectiveness of integrated care on CYP health, and in interpreting evidence from countries with different health systems to the UK.[66] A recent meta-analysis of randomized controlled studies evaluating the impact of these domains found improvement to quality of life amongst CYP using integrated models, but mixed evidence regarding the effect on health outcomes and service use.[280] However, a separate meta-analysis found that integrated care models were associated with improvements in health behaviours such as

smoking and substance misuse, and some mental health indicators.[281] Further, observational studies do suggest integration may reduce emergency activity,[282] and analyses from Paediatrics 2040 suggests conditions which may be suitable for primary care management to be contributing most to increased emergency healthcare activity shown in this chapter.[283] Improvements in capacity to manage these conditions outside hospital may dramatically reduce future demand on secondary services, and so increase ability to care for CYP who most need secondary care input.

Strengths and limitations

With near complete national coverage for inpatient secondary care in England, HES data can allow for powerful longitudinal analyses of healthcare activity. However, these data are not without limitations. The clinical data are crude, and accuracy, reliability and completeness vary across England, and between datasets, data fields, and over time.[165,170,174-178,181,182] The huge scale of these data can also present unique analytic problems; decisions over how to clean the data, link and characterise episodes of care and classify duplicates, affects millions of observations, and may have large impacts on these findings. There is also variation in coding accuracy by age group. For example, diagnostic certainty for asthma amongst children presenting with wheeze increases with age.[284] Declines in activity due to asthma I present here may reflect changes in coding practices, rather than a true reduction in asthma admissions.

Describing these data by cause in a meaningful way required developing a novel system of grouping cause of admission based on both GBD cause categories and ICD-10 chapter. Other methods to group causes, or classify type of admission, may have resulted in different estimates. Importantly however, I did not need to modify cause maps provided by the GBD to identify admissions due to epilepsy, diabetes and asthma, the chronic conditions of most interest to this thesis. Other limitations to this analysis include relying on documentation for *primary* cause of admission to classify each episode of care. A key limitation of this work is that I did not analyse data on trends for comorbidities, and so cannot capture patterns in admission amongst CYP with medical complexity, many of whom may have increased mortality risk.

Finally, I have only examined trends in emergency admissions, and have not described patterns of accident & emergency, primary care, or outpatient activity use. As capacity and barriers to accessing care in each part of the health system will affects all other areas,[276,277] it is difficult to interpret trends I present here in isolation. Including the full spectrum of health services in further analyses will place the results presented here in their wider context.

Conclusions

These findings show large changes to emergency hospital activity for CYP including for conditions where the UK has high mortality. There are multiple potential drivers to these trends, including the degree to which primary and secondary care services are integrated.

Understanding these patterns provides context for Chapter 8 of this thesis, where I will describe individual level analyses of survival of CYP after admission with epilepsy, asthma or diabetes. In this chapter I will analyse how socioeconomic and demographic factors, and markers of healthcare activity, are associated with increased mortality hazard, and may further indicate how better integration of health services could improve outcomes.

Chapter 8

Associations between healthcare activity amongst children and young people in England and epilepsy, asthma and diabetes mortality

Previous chapters in this thesis have identified factors which may be associated with the UK's high mortality for children and young people (CYP) compared with other high income countries. These include understanding the effect of geographic variation in mortality; although many regions of the UK have lower mortality than the best performing EU15+ countries, high mortality in some regions results in excess deaths nationally. Socioeconomic and demographic differences explain much of this variation, but these associations vary with age, as described in Chapter 6. Health service factors may also be important, and large changes to emergency admission rates in England described in Chapter 7 suggest there are opportunities to improve integration of primary and secondary paediatric services, but also across non health sectors. Individual analyses of patterns of healthcare activity prior to death may provide further insights regarding areas where health service reform may be beneficial, and identify opportunities to target additional services for CYP at most risk. This approach, using national data to inform the potential need for interventions at individual level, aligns with plans within the NHS Long Term plan to introduce *population health management* solutions to identify areas of greatest health need and match NHS services to meet them.[21]

In this chapter I use Hospital Episode Statistics (HES) data to identify cohorts of CYP admitted with asthma, epilepsy and diabetes; chronic conditions where the UK performs poorly. These data are linked to Office for National Statistics (ONS) mortality outcomes, which allow me to explore factors which may be associated with mortality hazard. I first assess associations between mortality and socioeconomic characteristics in CYP. In addition to age and sex, I explore associations between mortality and socioeconomic deprivation (measured by Index of Multiple Deprivation quintile category), geographic region, and ethnicity (where data allow).

I then use subsequent HES inpatient, outpatient and A&E records within each cohort to assess patterns of healthcare activity which may be associated with increased mortality hazard. I derived variables to assess health service use based on data availability within HES and previous work identifying concerning patterns of health care activity. Firstly, I considered further attendances to Accident and Emergency, or repeat emergency admissions due to the index cause (epilepsy, asthma or diabetes), to indicate some form of difficulty managing the chronic condition in the community, or an overall deterioration in health status. Secondly, I assessed associations between not being brought to appointments and mortality hazard amongst these CYP. Not attending planned outpatient care has previously been highlighted as a concern in Confidential Enquiry into Maternal and Child Health (CEMACH),[44] and in other studies.[273,285-287] Although the reasons for missing appointments are complex, and will include logistical and clerical errors, and improvement in health status, this may also represent vulnerability or disengagement with services.[89,288] Thirdly, mental health comorbidity has been shown to be prevalent in CYP with chronic conditions, including epilepsy and diabetes, and is associated with worse outcomes.[289-293] To investigate this amongst CYP I explored how *any* planned contact with mental health services identified within HES was associated with subsequent mortality hazard within each cohort.

Finally, I assessed how difficulty transitioning from paediatric to adult services amongst CYP with these chronic conditions may be associated with increased mortality hazard. Transition is defined in the Department of Health report *Transition: getting it right for younger people* as "a purposeful, planned process that addresses the medical, psychosocial and educational/vocational needs of adolescents and young adults with chronic physical and medical conditions as they move from child-centred to adult-oriented health care systems."[294] At a critical time in establishing independent chronic disease management, transition to adult services can present multiple challenges in sustaining engagement with services.[294-296] There is clear evidence that transition can be highly problematic for young people, and potentially result in poor health outcomes.[296-303] However, previous work in this area has rarely included population-level analyses, and the 2016 NICE guidance on transition identified the need for further longitudinal analyses of the health consequences of poorly facilitated transition.[295]

The Royal College of Paediatrics and Child Health (RCPCH) guidance on transition highlights five determinants of successful transition: develop a person-centred, developmentally appropriate plan; follow existing good practice guidelines; involve young people in decision making; share information between child and adult service; recognise the importance of service planners and commissioners on transition.[304] Available fields to assess these factors within HES were limited, but I hypothesized that an increased length of time in transitioning from paediatric to adult services may represent disengagement or poor planning, and so be associated with increased mortality hazard.

Chapter 8 methods

Data

I used HES data for emergency admissions, accident and emergency attendances, and outpatient appointments amongst 1-24 year olds in England from 2007 – 2018. Data permissions, cleaning and preparation are described in Chapter 2 and 7.

Admitted patient care

As described in chapter 7, the full admitted patient care (APC) data extract consisted of 12 years of data from 2007/08 to 2018/19, and 38,436,393 Finished Consultant Episodes (FCE). After cleaning procedures there were 32,277,081 FCEs available for analysis. Details of steps undertaken to clean the APC data, and assign type and cause of admission, are described in Chapter 7.

Accident and emergency

The full Accident and Emergency (A&E) HES dataset also consisted of 12 years of data 2007/08 to 2018/19, and 74,573,301 attendances. 1,490,819 observations were excluded as the usual place of residence was outside England. 1,342,030 observations were excluded as they related to planned attendances to A&E. 5,915,753 observations occurred after March 31st 2018 and were removed as only provisional estimates were available for this financial year, and a further 26,171,246 observations were removed as they occurred before 1st April 2012, the financial year in which the Accident and Emergency HES dataset was considered to have national coverage. Because attendances to A&E more than once on the same day may

represent real events, I did not drop duplicate observations by date in this dataset. This left 39,653,453 observations within the A&E dataset.

Outpatients

The full Outpatient dataset consisted of 12 years of data from 2007/8 to 2018/19, and 195,593,636 observations (planned outpatient clinics). 1,916,619 observations were removed as the usual place of residence was outside of England. 9,287,981 duplicate observations, where a patient had two appointments on the same date with the same specialty, were dropped, (appointments which were attended were prioritised). 15,111,106 observations were removed as they occurred during the financial year 2018/19, as only provisional estimates were available for this year. This left 169,277,930 observations.

Outpatient activity related to the index cause, and general appointments, were identified using the TRETSPEF and MAINSPEF fields within HES, relating to the specialty group the consultant was working under for that clinic, or contracted under overall, respectively. When assigning specialty to an outpatient clinic I prioritised the specialty within TRETSPEF, and only used MAINSPEF when TRETSPEF was missing.

Procedures

I created three cohorts of all CYP aged 1-24 admitted as an emergency due to epilepsy, asthma and diabetes, and explored hazard of death after first (index) admission.

Index admission and cohort definition

The three cohorts (epilepsy, asthma or diabetes) contained all CYP with an admission where the primary reason for admission was for that cause, and the index admission was the first of these admissions within each CYP. I used the following ICD10 codes to identify each cohort:

Epilepsy:	G40-G419; Z820
Asthma:	J45-J469; Z825
Diabetes:	E10-E101; P702; E103-E111; E113-E119; E123-E1311; E12-E121; E08-E0811; E083-E089; R73-R739; E133-E141; E143-E149

After identifying the index admission, all subsequent HES hospital activity records (admissions, accident and emergency contacts, outpatient contacts), were linked using the encrypted HES patient identifier provided by NHS digital, to enable different patterns of healthcare activity to be identified.

Follow up period

Data were available for admissions up to age 24 and between 2007 and 2018, linked to ONS mortality outcomes (date and cause of death) provided by HES. Patients who were less than 24 at their last appearance in any HES dataset were assumed to have been available for further hospital activity up to the day before their 25th birthday. However, as age was only recorded in years at the time of hospital activity, follow up time was defined as the number of days between the index admission and; 1) six months after the financial year in which the patient turned 24 or the last hospital activity record during their 24th year (whichever was later), 2) 31st March 2018 (the most recent reliable date for hospital activity); 3) date of death (when due to the index cause). Patients who died during the index admission were excluded.

Note some patients will have emigrated abroad after first appearing in the dataset. Although these patients were lost to follow up, I was unable to reliably identify them, and so they continued to be considered within the population at risk.

Baseline characteristics: time invariant predictors of survival

Sex, ethnicity, usual place of residence, and socioeconomic status of patients, were defined and cleaned using data provided across all three HES datasets as follows.

Sex

Sex was coded as 1 = male, 2 = female. Where sex was recorded differently within the same individual across hospital contacts used the most common non-missing value for all observations for that patient. CYP where sex was unspecified (across all HES datasets) were dropped.

Ethnicity

Where ethnicity differed across HES datasets, this was replaced with the most common non-missing ethnic category recorded (i.e. the mode). Ethnicity was defined using a dichotomous variable and coded as either 0 = "White" or 1 = "Black, Asian or Minority Ethnic group (BAME)."

Geographic Region

Usual place of residence was determined by patient postcode at the time of the index admission, and categorized in to the 9 Government Office Regions (North East, North West, Yorkshire and Humber, East Midlands, West Midlands, East of England, London, South East, South West). CYP usually resident outside of England were excluded.

Socioeconomic status

Index of Multiple Deprivation (IMD) quintile category at the time of the index admission was used to define socioeconomic status of CYP. As described in Chapter 6, IMD is a measure of relative deprivation by Lower Super Output Area (LSOA), and is based on the following area level indicators: income deprivation; employment deprivation; education, skills and training deprivation; health deprivation and disability; crime; barriers to housing and services; living environment deprivation.[217]

Hospital activity after the index admission: time variant predictors of survival

Subsequent admissions

The cumulative number of further emergency admissions due to the index cause (epilepsy, diabetes or asthma). This was defined as a categorical variable and coded as: 0 "No further admissions"; 1 "2-4 admissions"; 2 "5 or more admissions."

Attendances to accident and emergency

The cumulative number of emergency attendances to A&E following the index admission. Note these could be associated with a subsequent admission with the index cause, or an attendance to A&E for any other reason, as diagnosis at A&E attendance is poorly recorded within HES. A&E attendances were defined as a categorical variable and coded as 0 "up to 1

further attendance to A&E" or 1 "more than 1 attendance to A&E". Associations between A&E attendances and mortality could only be assessed within a subset of each cohort where the index admission occurred after March 31st 2012 (the date from which A&E dataset was considered to reach national coverage).

Mental health contacts

Any planned or unplanned contact with mental health services after the index admission. This was defined as a dichotomous variable and coded as 0 = "no mental health contact" and 1 = "mental health contact." Participants were considered to have had contact with mental health services if they had either:

1) an inpatient admission where the primary diagnosis within chapter 5 of ICD 10 (Mental and Behavioural Disorders, codes F00 – F99)

or

2) an inpatient admission or outpatient appointment (including those attended / not attended or cancelled) where the treatment or main specialty of the responsible consultant was defined as follows, with associated HES code also shown:

   child and adolescent psychiatry [711]
   clinical psychology [656]
   adult mental illness [710]
   forensic psychiatry [712]
   psychotherapy [713]
   old age psychiatry [715]
   eating disorders [720]
   addiction services [721]
   liaison psychiatry [722]
   psychiatric intensive care [723]
   perinatal psychiatry [724]
   mental health recovery and rehabilitation service [725]
   mental health dual diagnosis service [726]

Not being brought to appointments

This was defined as any planned outpatient appointment associated with the index admission which was not attended. These appointments could be either general medicine, general paediatric, or specialist clinic codes associated with each cohort, defined as follows with associated HES code:

Epilepsy: Paediatric epilepsy [223], paediatric neuro-disability [291], paediatric neurology [421], adult neurology [400]

Asthma: Paediatric respiratory medicine [258], respiratory medicine [304], thoracic medicine [340], respiratory physiology [341]

Diabetes: Paediatric diabetic medicine [263], paediatric endocrinology [252], diabetic medicine [307], endocrinology [302]

Participants were defined as either 0 = "no appointments not attended" or 1 = "appointment not attended." The number of offered appointments was associated with not attending an appointment, reflecting length of follow up. To adjust for this, I included a continuous variable of the total number of offered appointments at the time when the first appointment was not attended. Appointments which were not attended during an inpatient admission were excluded.

Transitioning to adult services

I defined those who had transitioned to adult services as participants who had:

1) Any planned paediatric healthcare activity associated with the index admission. This could be either a planned inpatient paediatric admission or attending a paediatric outpatient appointment associated with the index admission. Within each cohort, I defined this using the same outpatient appointment codes as when analysing *not attending appointments* described above.

and

2) Any **planned** adult healthcare activity after the last planned paediatric healthcare activity. This could be a planned inpatient admission associated with the index

admission, or attending an adult appointment either in general medicine or a clinic code associated with the index admission described above.

Within this sub-sample, I analysed hazard of death amongst those who had transitioned within 6 months, (i.e. where subsequent planned adult healthcare activity was at least 6 months after the last paediatric health care activity), compared with those who had taken at least 6 months to transition to adult services. Emergency adult activity was not included here as this might be an indicator of poor transition. Transition was coded as 0 = "transition within 6 months" 1 = "transition longer than 6 months."

Statistical analysis

As follow-up time varied in these cohorts, and to account for censored participants, I used cox regression models to assess survival after the index admission, as described by Singer and Willet.[305] Time was measured in days from index admission to outcome (death), or end of follow up as described above. Predictors of survival in these models were baseline demographic characteristics (time invariant exposures), and subsequent hospital activity (time variant exposures). Where time variant exposures occurred on the same day, I prioritised clinical activity as follows: where emergency admissions occurred on the same day as an outpatient clinic or A&E attendance, only the emergency admission was counted; where an A&E attendance occurred on the same day as an outpatient appointment, only the A&E attendance was counted. I tested if the proportional hazards assumption was valid in each model using the *estat phtest* command in Stata.

I first ran univariable models for each background variable and healthcare activity. I then selected background variables which may confound any observed associations between healthcare activity and hazard of death to include in a multivariable model. Age and sex were defined as important predictors of survival a priori. Other variables which were found to be significantly associated with hazard of death in the univariable analysis were added in a stepwise fashion. I assessed if adding additional predictors improved model fit using likelihood ratio tests (LRT), Akaike information criterion (AIC) and Bayesian information criterion (BIC). Participants with missing data for IMD were excluded to enable nested models to be assessed. In view of the large changes over time in both mortality and admission rates

for asthma, epilepsy and diabetes described in Chapters 3 and 7, and to address possible cohort effects, I adjusted these analyses for admission year.

Sensitivity analyses

Excluding those without subsequent healthcare activity

A substantial proportion of participants had no further healthcare activity after the index admission. This highlights a main limitation of this analysis; that I was unable to capture healthcare contact within General Practice with these data. However, this may also reflect issues around case definition specificity, with some CYP not coded correctly for an admission, and so then not requiring further secondary care input. To assess this, I repeated the analysis excluding all participants with only one healthcare episode in the dataset.

Stratifying by age

The presentation, management and healthcare activity patterns for the chronic conditions I analysed are known to differ by age. Although age at presentation was included within each model, I assessed this further by repeating the analyses in different age groups within each cohort.

Within the epilepsy cohort I analysed children (1-9) and adolescents (10-24) separately, to reduce the likelihood of including children with febrile convulsions, and to reflect differences in the presentation and management in these age groups.[306,307] Similarly, some presentations with diabetes in very young children may reflect separate clinical entities to those diagnosed in adolescence. I therefore restricted the repeat analysis to 10-24 only; I was unable to assess 1-9 separately within diabetes as there were too few children. Within the asthma cohort, I repeated the analysis excluding those aged under 5. I did this to reflect challenges in diagnosing asthma in pre-school children, where presentations with wheeze from other causes create diagnostic uncertainty.[284]

Excluding general paediatric outpatient activity

I initially analysed outpatient clinic activity for not attending appointments and transition to adult services using both general clinics and specialist codes. This broad case definition

assumes general outpatient activity was for the purpose of managing epilepsy, asthma or diabetes within each cohort, rather than any other co-morbidity. To reduce the likelihood of capturing outpatient activity not related to the index cause, I repeated these analyses as follows:

- I assessed associations with not attending appointments and death using only specialist outpatient codes related to the index admission in either adults or paediatrics within each cohort.
- I assessed associations with length of transition to adult services and death defining the last paediatric clinic appointment using only specialist clinic codes related to the index admission. Note the first adult appointment could still be in a general clinic.

Table 33: Background characteristics within each cohort (epilepsy, asthma, diabetes mellitus)

	Epilepsy		Asthma		Diabetes Mellitus	
	n	percent	n	percent	n	percent
Participants	46803		176006		54519	
Outcome						
Survived until censored	45277	(96.7)	175541	(99.7)	54218	(99.4)
Died	1526	(3.3)	465	(0.3)	301	(0.6)
Deaths due to admission	350	(22.9)	169	(36.3)	143	(47.5)
Deaths due to other cause	1176	(77.1)	296	(63.7)	158	(52.5)
Age group						
1 to 4	10672	(22.8)	67558	(38.4)	5353	(9.8)
5 to 9	8486	(18.1)	48051	(27.3)	9866	(18.1)
10 to 14	7656	(16.4)	22741	(12.9)	15111	(27.7)
15 to 19	9643	(20.6)	17074	(9.7)	13204	(24.2)
20 to 24	10346	(22.1)	20582	(11.7)	10985	(20.1)
Sex						
Male	25319	(54.1)	101945	(57.9)	28933	(53.1)
Female	21484	(45.9)	74061	(42.1)	25586	(46.9)
Region						
North East	2488	(5.3)	9032	(5.1)	3026	(5.6)
North West	7045	(15.1)	33457	(19.0)	7873	(14.4)
Yorkshire and Humber	5425	(11.6)	17463	(9.9)	5498	(10.1)
East Midlands	3668	(7.8)	11662	(6.6)	4689	(8.6)
West Midlands	5442	(11.6)	22846	(13.0)	5846	(10.7)
East of England	4575	(9.8)	15492	(8.8)	6195	(11.4)
London	7376	(15.8)	28676	(16.3)	7412	(13.6)
South East	6637	(14.2)	22703	(12.9)	8733	(16.0)
South West	4147	(8.9)	14675	(8.3)	5247	(9.6)
Index of Multiple						
1 (most deprived)	14376	(30.7)	58424	(33.2)	13481	(24.7)
2	10826	(23.1)	40009	(22.7)	11529	(21.1)
3	8386	(17.9)	30487	(17.3)	10257	(18.8)
4	7021	(15.0)	25270	(14.4)	9681	(17.8)
5 (least deprived)	6172	(13.2)	21786	(12.4)	9559	(17.5)
missing	22	(0.0)	30	(0.0)	12	(0.0)
Ethnicity						
White	33529	(71.6)	112531	(63.9)	42910	(78.7)
BAME	9145	(19.5)	47643	(27.1)	7298	(13.4)
missing	4129	(8.8)	15832	(9.0)	4311	(7.9)

Table 34: Healthcare activity within each cohort (epilepsy, asthma and diabetes mellitus)

	Epilepsy		Asthma		Diabetes Mellitus	
	n	percent	n	percent	n	percent
Mental health contacts						
No contact planned	39923	(85.3)	167766	(95.3)	47243	(86.7)
1 or more contact planned	6880	(14.7)	8240	(4.7)	7276	(13.3)
Admissions with index cause						
No further admissions	25758	(55.0)	123298	(70.0)	34077	(62.5)
2-4 further admissions	14745	(31.5)	43069	(24.5)	14913	(27.4)
5 or more further admissions	6300	(13.5)	9639	(5.5)	5529	(10.1)
Outpatient care including general appointments						
No appointments planned	4672	(10.0)	72353	(41.1)	2913	(5.3)
1 or more appointments planned	42131	(90.0)	103653	(58.9)	51606	(94.7)
No appointments not attended	19832	(47.1)	53308	(51.4)	16417	(31.8)
1 or more appointments not attended	22299	(52.9)	50345	(48.6)	35189	(68.2)
Outpatient care excluding general appointments						
No appointments planned	12225	(26.1)	136136	(77.3)	7424	(13.6)
1 or more appointments planned	34578	(73.9)	39870	(22.7)	47095	(86.4)
No appointments not attended	19369	(56.0)	19967	(50.1)	16610	(35.3)
1 or more appointments not attended	15209	(44.0)	19903	(49.9)	30485	(64.7)
Transition to adult services						
Data not available for transition	41048	(87.7)	172842	(98.2)	43482	(79.8)
Data available for transition	5755	(12.3)	3164	(1.8)	11037	(20.2)
Data not available for transition (excl general paediatric appointments)	43053	(92.0)	174388	(99.1)	47088	(86.4)
Data available for transition (excl general) paediatric appointments)	3750	(8.0)	1618	(0.9)	7431	(13.6)
Accident and Emergency						
0-1 attendances	11617	(51.6)	52034	(59.4)	18943	(69.8)
2 or more attendances	10899	(48.4)	35586	(40.6)	8181	(30.2)

Chapter 8 results

Table 33 (p.239) describes background characteristics of participants in each cohort, with these data also shown as visual summaries below figures 59 (p.242), 60 (p.249) and 61 (p.256).Table 34 (p.240) describes healthcare activity for participants within each cohort.

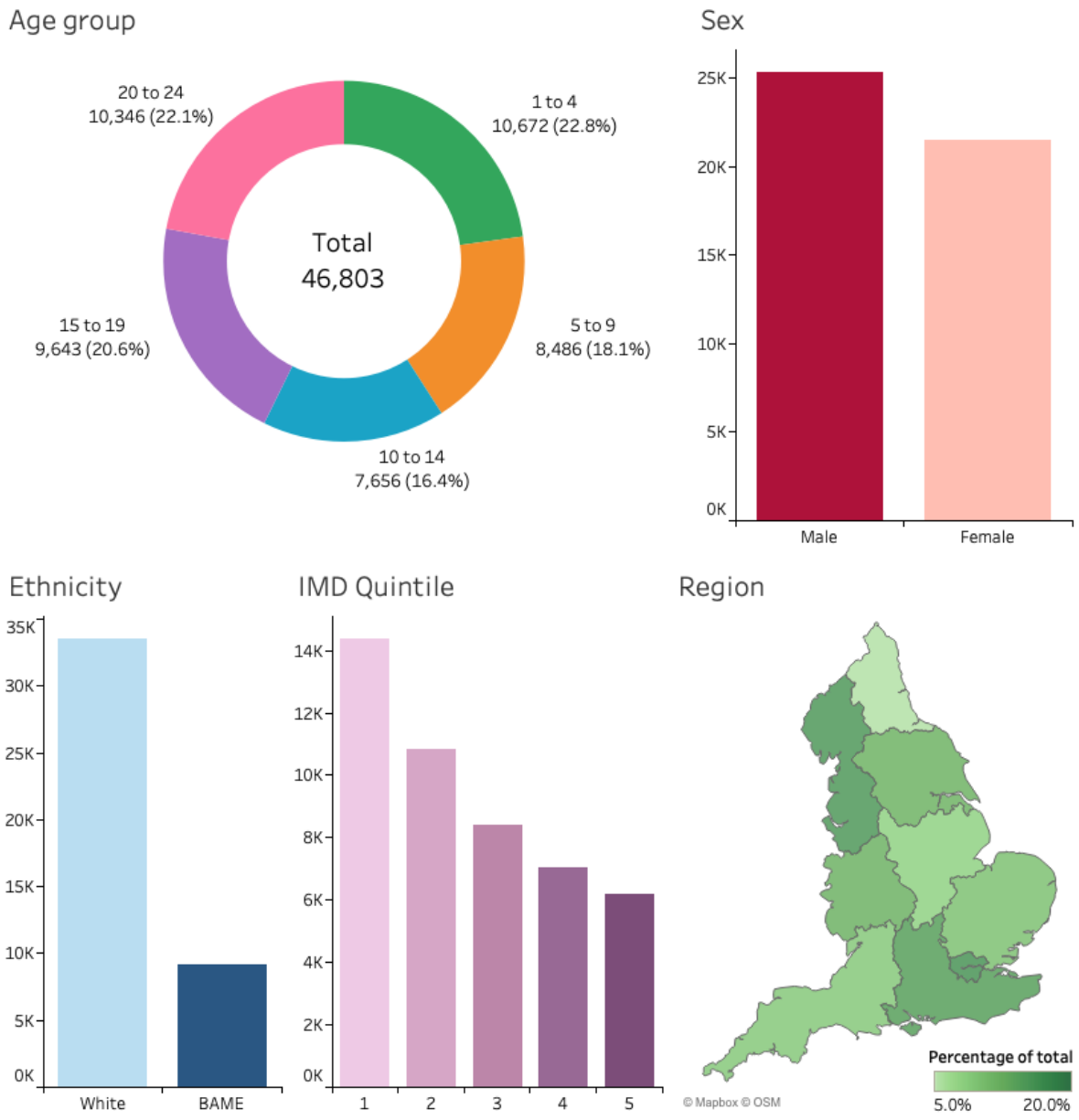
Epilepsy

The epilepsy cohort included 46,803 participants. 54.1% were male and 71.6% were white. 22.8% were aged 1-4, 22.1% were 20-24, 20.6% were 15-19, 18.1% were 5-9 and 16.4% were 10-14. The region with the most participants was London with 7376 (15.8% of the total), compared with only 2488 from North East (5.3% of the total). 30.7% of participants lived in the most deprived IMD quintile category, compared with 13.2% living in the least deprived quintile category (Figure 59).

The epilepsy cohort contained 1526 deaths (3.3% of the total), of which 350 had epilepsy as the primary cause of death (22.9% of deaths). Median length of follow up was 1644 days [range 1 – 4391 days]. Overall 5-year survival following the index admission was 99.2% for all causes of death, and 99.6% where epilepsy was the primary cause of death.

The epilepsy cohort contained 1,743,451 healthcare contacts (including the index admission). 58.8% of the cohort had at least 2 attendances to A&E during follow up, and 45% had at least 2 further emergency admissions with epilepsy. 14.7% had some form of contact with mental health services. 90.0% of participants were offered an outpatient appointment in either a general or specialist epilepsy clinic, and of these 52.9% did not attend on at least one occasion. 73.9% of participants were offered an appointment in a specialist epilepsy clinic, and of these 44.0% did not attend on at least one occasion. During follow up, 12.3% of the cohort transitioned to adult services when general paediatric appointments were included in this definition. 8.0% transitioned to adult services when only specialist paediatric epilepsy clinics were used for this definition (table 34, p.240).

Figure 59: Epilepsy cohort visual summary of background characteristics



Epilepsy cohort univariable analysis

Output from the univariable cox regression analysis is shown in table 35 (p.245). Participants who entered the study later had a lower hazard of death than those who entered in 2007 (HR 0.86 [0.82 – 0.90] $p < 0.001$ for each additional year of entry after 2007). Increasing age at entry in to the study in years was associated with significantly higher hazard of death (HR1.06 [1.04 – 1.08], $p < 0.001$). Participants living in the South West had significantly higher hazard

of death compared with those living in the North East, although this was borderline (HR1.93 [1.01 – 3.69], p=0.047).

The following healthcare contacts were associated with significantly higher hazard of death due to epilepsy : additional admissions with epilepsy (2-4 further admissions HR 2.50 [1.95 – 3.20] p<0.001, 5 or more further admissions HR 5.10 [3.77 – 6.89], p<0.001), not attending a planned outpatient appointment (including general appointments HR1.47 [1.12 – 1.92], p =0.005, excluding general appointments HR1.72 [1.29 – 2.30], p<0.001), having more than 1 subsequent attendance to A&E (HR1.97 [1.15 – 3.37], p=0.01). Taking greater than 6 months to transition to adult services was also associated with increased hazard of death, (only when general paediatric appointments were excluded) (HR 2.84 [1.37 – 5.91], p=0.005). The proportional hazards assumption was shown to be valid for each univariable model (phTest >=0.05).

Epilepsy cohort multivariable analysis

Table 36 (p.246) shows the output for assessing model fit used for the multivariable analysis. Compared with model A (with only year at entry included as a covariate), only the addition of age at index admission significantly improved model fit. However, due to the importance of deprivation, sex and age to describe variation in mortality described previously, model D was selected to describe hazard of death related to background characteristics. Region was excluded as although CYP residents in the South West were shown to have increased hazard of death compared to those in the North East, this was borderline and including this did not improve model fit.

Healthcare contacts and hazard of death within the Epilepsy cohort

Table 37 (p.247) shows multivariable regression output for the epilepsy cohort following the addition of time varying predictors of survival related to healthcare use. After adjusting for year of entry to the study, age at entry, sex and IMD, hazard for death was significantly increased among those who: went on to have subsequent admissions with epilepsy (1-4 further admissions HR 2.75 [2.14-3.53], p<0.001; 5 or more admissions HR 6.08 [4.47 – 8.27], p<0.001); did not attend a planned outpatient appointment (including general appointments

HR 1.31 [1.0-1.7], p=0.049, excluding general appointments (HR 1.41 [1.05 – 1.90], p = 0.02); took more than six months to transition to adult services, but only when general paediatric appointments were excluded (HR 2.33 [1.11-4.89], p = 0.03). Although attending A&E on more than one occasion during follow up was also associated with increased hazard of death, the proportional hazards assumption for this model was invalid after the addition of background variables (phTest = 0.01), and so the output is unreliable and difficult to interpret.

Results from the sensitivity analysis were similar. When the analysis was limited to 1 to 9 year olds, the following healthcare activity was associated with increased hazard of death: further admissions with epilepsy (2-4 admissions HR 3.74 [2.17 – 6.45], p<0.001; 5 or more admissions HR 8.74 [4.73 – 16.12], p<0.001); not attending a planned appointment, but only when general appointments were included (HR 1.69 [1.01 – 2.83], p=0.04). When the analysis was limited to 10-24, only further admissions with epilepsy was significantly associated with increased hazard of death (2 – 4 admissions HR 2.50 [1.88 – 3.32], p<0.001, 5 or more admissions HR 5.41 [3.76 – 7.78, p<0.001). I did not repeat the transition analysis stratified by age. There were no meaningful differences to the results when participants with only one observation were excluded.

Table 35: Univariable cox regression output for the epilepsy cohort. Hazard of death due to epilepsy by baseline characteristics and healthcare activity

	Epilepsy deaths				
	HR	lower	upper	p	PhTest p
Background variables					
Year of entry	0.86	0.82	0.90	<0.001	0.49
Age in years	1.06	1.04	1.08	<0.001	0.08
Female sex	0.94	0.76	1.16	0.58	0.36
IMD quintile (baseline most deprived)					
2	1.01	0.77	1.34	0.92	0.18
3	0.83	0.60	1.14	0.25	
4	0.83	0.59	1.17	0.29	
5	0.96	0.69	1.35	0.83	
English region (baseline North East)					
North West	1.73	0.93	3.22	0.08	0.77
Yorkshire and Humber	1.48	0.77	2.82	0.24	
East Midlands	1.50	0.75	2.96	0.25	
West Midlands	1.21	0.62	2.34	0.58	
East of England	1.55	0.80	3.00	0.19	
London	1.52	0.81	2.85	0.19	
South East	1.86	1.00	3.47	0.05	
South West	1.93	1.01	3.69	0.047	
BAME ethnicity	1.00	0.73	1.36	0.99	0.27
Healthcare contacts					
Mental health contact	1.27	0.92	1.76	0.14	0.40
2 -4 further admissions	2.50	1.95	3.20	<0.001	0.25
5 or more further admissions	5.10	3.77	6.89	<0.001	
Not attending appointment	1.47	1.12	1.92	0.005	0.26
Not attending appointment (excl general)	1.72	1.29	2.30	<0.001	0.73
Transition > 6 months	1.62	0.93	2.83	0.09	0.78
Transition > 6 months (excl general)	2.84	1.37	5.91	0.005	0.88
More than 1 attendance to A&E	1.97	1.15	3.37	0.013	0.07

Table 36: Model selection for time invariant predictors: Epilepsy cohort (deaths due to epilepsy)

	Model A				Model B				Model C				Model D				Model E			
	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.86	0.82	0.90	0.00	0.86	0.83	0.90	0.00	0.86	0.82	0.90	0.00	0.86	0.82	0.90	0.00	0.86	0.82	0.90	0.00
Age in years					1.06	1.04	1.07	0.00	1.06	1.04	1.08	0.00	1.06	1.04	1.08	0.00	1.06	1.04	1.07	0.00
Female sex									0.92	0.74	1.13	0.43	0.92	0.74	1.13	0.43	0.92	0.74	1.13	0.42
IMD (Most deprived)																				
2													1.01	0.76	1.34	0.94	0.95	0.72	1.27	0.74
3													0.82	0.60	1.13	0.23	0.75	0.54	1.05	0.09
4													0.83	0.59	1.17	0.28	0.75	0.53	1.06	0.10
5													0.98	0.70	1.37	0.91	0.86	0.60	1.22	0.39
Region (North East)																				
North West																	1.66	0.89	3.10	0.11
Yorkshire & Humber																	1.53	0.80	2.92	0.20
East Midlands																	1.60	0.80	3.17	0.18
West Midlands																	1.23	0.63	2.39	0.54
East England																	1.77	0.91	3.44	0.09
London																	1.60	0.85	2.99	0.14
South East																	2.09	1.11	3.92	0.02
South West																	2.07	1.08	3.98	0.03
AIC	7165.32				7122.19				7123.57				7128.81				7133.71			
BIC	7177.72				7146.99				7160.76				7215.60				7319.68			
PhTest p	0.49				0.15				0.20				0.13				0.41			
LRT p					0.00				0.43				0.60				0.20			

Table 37: Cox regression output for hazard of death associated with epilepsy following healthcare (time varying) predictors and adjusted for background variables

	Mental Health				Further admissions				Not attending outpatients				Transition with general paediatrics				A&E attendances			
	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.86	0.82	0.90	<0.001	0.88	0.84	0.92	<0.001	0.87	0.83	0.92	<0.001	0.99	0.85	1.14	0.84	0.93	0.78	1.11	0.42
Age in years	1.06	1.04	1.07	<0.001	1.07	1.06	1.09	<0.001	1.06	1.04	1.08	<0.001	1.25	1.11	1.41	<0.001	1.04	1.00	1.07	0.03
Female sex	0.92	0.74	1.13	0.42	0.90	0.73	1.12	0.35	0.94	0.75	1.18	0.60	1.08	0.64	1.84	0.76	0.77	0.48	1.25	0.29
IMD (Most deprived)																				
2	1.01	0.77	1.34	0.93	1.03	0.78	1.37	0.81	0.95	0.70	1.29	0.76	0.72	0.34	1.55	0.40	1.42	0.75	2.72	0.28
3	0.82	0.60	1.14	0.24	0.85	0.61	1.17	0.31	0.85	0.61	1.19	0.35	0.60	0.25	1.42	0.25	1.08	0.51	2.29	0.84
4	0.83	0.59	1.17	0.28	0.84	0.60	1.18	0.31	0.79	0.54	1.14	0.20	0.71	0.31	1.63	0.43	1.44	0.69	2.99	0.33
5	0.98	0.70	1.37	0.91	1.01	0.72	1.41	0.96	0.88	0.61	1.29	0.52	1.10	0.52	2.31	0.80	1.38	0.63	2.99	0.42
Mental Health	1.15	0.83	1.59	0.39																
Further admissions																				
2-4					2.75	2.14	3.53	<0.001												
> = 5					6.08	4.47	8.27	<0.001												
Not attending op									1.31	1.00	1.70	0.049								
Transition													1.28	0.74	2.24	0.38				
A&E attendance																	1.98	1.16	3.38	0.01
phTest	0.16				0.14				0.13				0.60				0.01			

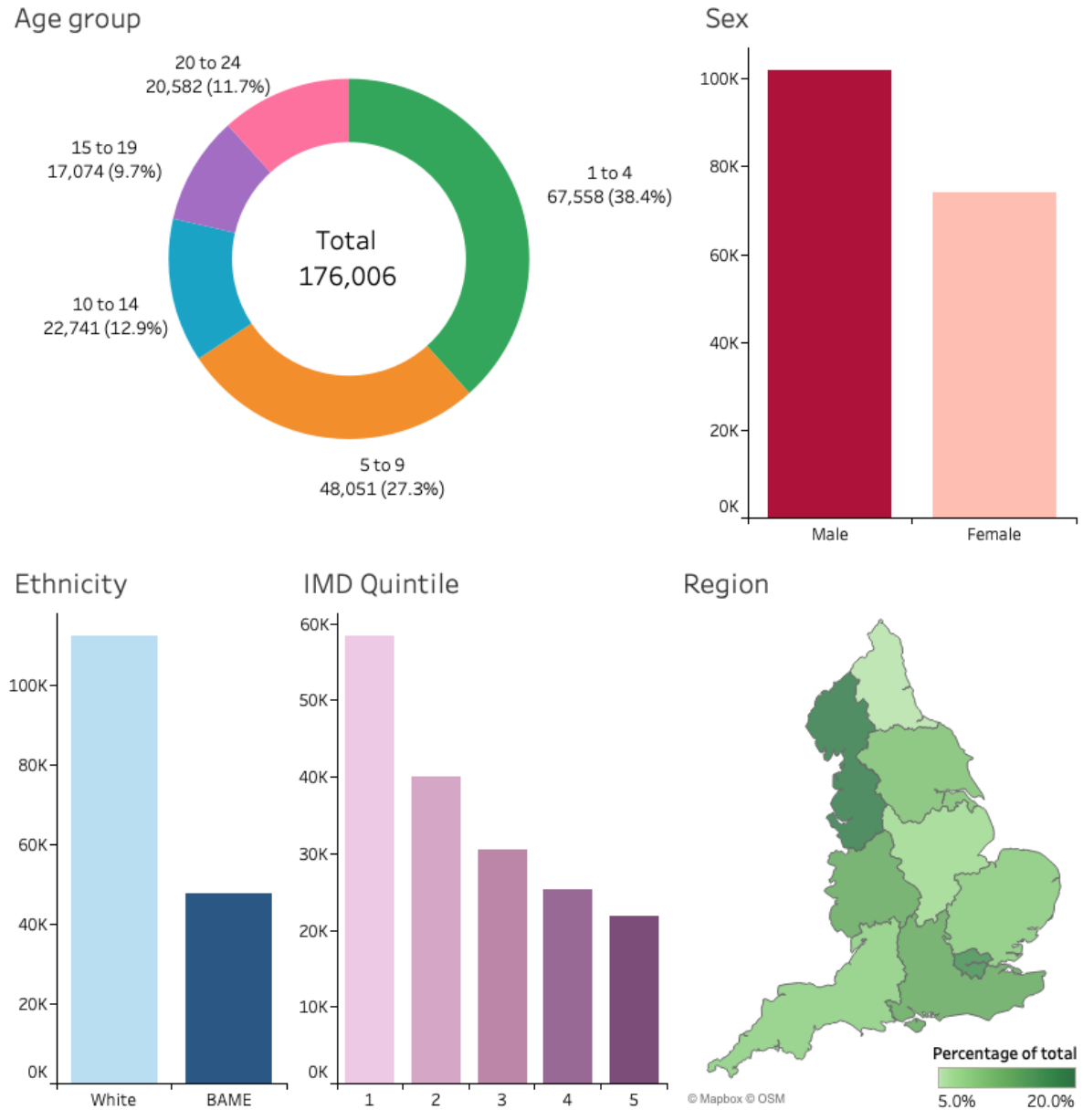
Table 37 (continued) Cox regression output for hazard of death associated with epilepsy following healthcare (time varying) predictors and adjusted for background variables

	Not attending outpatients (excl general paediatrics)				Transition (excl general paediatrics)			
	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.88	0.83	0.93	<0.001	0.95	0.79	1.14	0.59
Age in years	1.06	1.03	1.08	<0.001	1.19	1.04	1.36	0.01
Female sex	0.96	0.75	1.23	0.74	1.27	0.65	2.47	0.48
IMD (Most deprived)								
2	0.90	0.64	1.26	0.54	0.85	0.34	2.13	0.72
3	0.79	0.54	1.16	0.23	0.55	0.18	1.69	0.30
4	0.83	0.56	1.23	0.35	0.64	0.21	1.96	0.43
5	0.92	0.62	1.37	0.67	1.04	0.41	2.62	0.93
Not attending op	1.41	1.05	1.90	0.02				
Transition					2.33	1.11	4.89	0.03
phTest	0.42				0.39			

Asthma

The asthma cohort contained 176,006 participants. 57.9% were male and 63.9% were white (ethnicity data were missing in 9.0%). 38.4% of participants were aged 1-4 at the index admission; 27.3% were 5-9, 12.9% were 10-14, 11.7% were 20-24 and 9.7% were 15-19. 33.2% of participants lived in the most deprived IMD quintile category, and 12.4% in the least deprived quintile category. The region with the most participants was the North West with 33457 (19.0%), and the region with the least participants was the North East with 9032 (5.1%) (figure 60).

Figure 60: Asthma cohort visual summary of background characteristics



Description of the asthma cohort

Within the asthma cohort there were 465 deaths, of which 169 (36.3%) had asthma as the primary cause of death. Overall 5-year survival was 99.7% for all causes of death and 99.9% for asthma related deaths. The asthma cohort contained 3,179,043 healthcare contacts and median follow up time was 7.1 years (range 1 day – 12.4 years). 29.9% of participants had at least 2 further admissions with asthma during follow up, and 5.5% had 5 or more admissions. 58.9% had a planned outpatient follow up (including general clinics), and 48.6% of these did not attend at least one planned appointment. 22.7% had a planned specialist respiratory appointment, and 49.9% did not attend on at least one occasion. 3164 (1.8%) of participants were defined as having transitioned to adult services when general paediatric clinics were included in this definition, and 1618 (0.9%) participants transitioned to adult services when general paediatric clinics were excluded. 4.7% of participants had some form of mental health contact during follow up. 40.6% had at least 2 further attendances to A&E (table 34, p.240).

Asthma cohort univariable analysis

Output from the univariable cox regression analysis is shown in table 38 (p.252). Index year was significantly associated with decreased hazard of death (HR 0.92 [0.86 – 0.98], p =0.01 for each additional year of entry to the study after 2007) and age was significantly associated with increased hazard of death (HR1.08 [1.06 – 1.11], p<0.001). No other background variables were significantly associated with hazard for death. The following markers of healthcare activity were significantly associated with hazard of death: having further admissions with asthma (2-4 admissions HR 4.02 [2.75-5.97], p<0.001; 5 or more admissions HR 28.87 [18.92 – 44.06], p<0.001); having any contact with mental health services (HR 2.08 [1.09 – 3.96], p=0.026); not attending a planned specialist or general clinic (HR 2.06 [1.39 – 3.06], p<0.001); having more than 1 attendance to A&E during follow up (HR 2.69 [1.33 – 5.45], p=0.006)

Asthma cohort multivariable analysis

Table 39 (p.253) shows the output for assessing model fit for the asthma cohort. Similar to the epilepsy cohort, only the addition of age to the baseline model A (where year of entry to the cohort was the only predictor), was shown to significantly improve the model. However,

model D was again selected to adjust for background characteristics of participants amongst the asthma cohort, owing to the importance of sex and deprivation in describing patterns of wheeze in CYP.[308] As region was not significantly associated with hazard of death in the univariate analysis (in contrast to the epilepsy cohort), this was not included when assessing model fit.

Healthcare contacts and hazard of death within the asthma cohort

Table 40 (p.254) shows cox regression output for each healthcare activity adjusted for background characteristics of participants. After adjusting for year of entry in to the study, age, sex and IMD, the following healthcare activities were significantly associated with hazard of death due to asthma: further admissions with asthma (2-4 admissions HR 4.67 [3.18 – 6.85], p<0.001, 5 or more admissions HR 31.28 [20.36 – 48.04], p<0.001); at least 2 further attendances to A&E (HR 2.59 [1.27 – 5.25], p=0.01), not attending a specialist or general clinic (HR 1.66 [1.11 – 2.46], p=0.01). Results were similar for the sensitivity analyses, when children aged 1-4 were excluded, and when those with no further healthcare contacts after the index admission were excluded. The proportional hazards assumption was shown to be valid in all univariable and multivariable analyses undertaken (phtest p>=0.05).

Table 38 Univariable cox regression output for the asthma cohort. Hazard of death due to asthma by baseline characteristics and healthcare activity

	Asthma deaths				
	HR	lower	upper	p	PhTest p
Background variables					
Year of entry	0.92	0.86	0.98	0.008	0.76
Age in years	1.08	1.06	1.11	<0.001	0.61
Female sex	1.31	0.97	1.77	0.08	0.95
IMD quintile (baseline most deprived)					
2	0.74	0.49	1.12	0.16	0.12
3	0.99	0.65	1.49	0.95	
4	0.73	0.45	1.19	0.21	
5	0.60	0.34	1.05	0.07	
English region (baseline North East)					
North West	1.06	0.49	2.29	0.89	0.69
Yorkshire and Humber	1.14	0.50	2.63	0.76	
East Midlands	1.05	0.42	2.62	0.91	
West Midlands	1.43	0.66	3.14	0.37	
East of England	1.10	0.47	2.60	0.82	
London	1.00	0.45	2.23	0.99	
South East	1.06	0.47	2.38	0.90	
South West	0.76	0.30	1.92	0.56	
BAME ethnicity	1.06	0.72	1.55	0.78	0.27
Healthcare contacts					
2 -4 further admissions	4.02	2.75	5.87	<0.001	0.89
5 or more further admissions	28.87	18.92	44.06	<0.001	
Mental health contact	2.08	1.09	3.96	0.026	0.14
Not attending appointment	2.06	1.39	3.06	<0.001	0.28
Not attending appointment (excl general)	1.48	0.91	2.40	0.12	0.51
More than 1 attendance to A&E	2.69	1.33	5.45	0.006	0.78
Transition > 6 months	0.80	0.26	2.52	0.71	0.13
Transition > 6 months (excl general)	0.97	0.23	4.05	0.97	0.05

Table 39: Model selection for time invariant predictors: Asthma cohort (deaths due to asthma)

	Model A				Model B				Model C				Model D			
	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.92	0.86	0.98	0.01	0.92	0.86	0.98	0.01	0.92	0.86	0.98	0.01	0.92	0.86	0.98	0.01
Age in years					1.08	1.06	1.11	0.00	1.08	1.06	1.11	0.00	1.08	1.06	1.11	0.00
Female sex									1.07	0.79	1.46	0.67	1.07	0.78	1.46	0.67
IMD (Most deprived)																
2													0.73	0.48	1.11	0.14
3													0.98	0.65	1.48	0.91
4													0.72	0.44	1.17	0.19
5													0.59	0.34	1.04	0.07
Region (North East)																
North West																
Yorkshire & Humber																
East Midlands																
West Midlands																
East England																
London																
South East																
South West																
AIC	3941.61				3899.05				3900.86				3902.94			
BIC	3954.58				3924.99				3939.78				3993.74			
PhTest p	0.76				0.82				0.89				0.32			
LRT p					0.00				0.67				0.20			

Table 40: Cox regression output for hazard of death due to asthma following healthcare contacts and adjusted for background variables

	Mental Health				Further admissions				Not attending outpatients				Transition with general paediatrics				A&E attendances			
	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.92	0.86	0.98	0.01	0.96	0.90	1.02	0.15	0.89	0.82	0.97	0.01	1.17	0.87	1.59	0.30	0.85	0.68	1.06	0.14
Age in years	1.08	1.06	1.11	<0.001	1.10	1.07	1.12	<0.001	1.09	1.06	1.12	<0.001	1.07	0.90	1.27	0.44	1.07	1.02	1.11	<0.001
Female sex	1.07	0.78	1.46	0.68	0.91	0.66	1.24	0.55	1.13	0.78	1.64	0.53	4.57	1.00	20.86	0.05	1.38	0.73	2.58	0.32
IMD (Most deprived)																				
2	0.73	0.48	1.11	0.14	0.75	0.50	1.14	0.18	0.63	0.38	1.05	0.07	0.34	0.07	1.58	0.17	1.30	0.50	3.37	0.59
3	0.98	0.65	1.48	0.92	1.05	0.70	1.59	0.81	0.93	0.57	1.51	0.77	0.21	0.03	1.66	0.14	3.22	1.41	7.35	0.01
4	0.72	0.44	1.18	0.19	0.77	0.47	1.26	0.30	0.56	0.30	1.05	0.07	0.25	0.03	2.00	0.19	1.63	0.58	4.58	0.36
5	0.60	0.34	1.04	0.07	0.66	0.37	1.15	0.14	0.45	0.21	0.95	0.04	0.28	0.03	2.25	0.23	1.29	0.40	4.19	0.67
Mental Health	1.54	0.80	2.94	0.19																
Further admissions																				
2-4					4.67	3.18	6.85	<0.001												
> = 5					31.28	20.36	48.04	<0.001												
Not attending op									1.66	1.11	2.46	0.01								
Transition													0.72	0.23	2.30	0.58				
A&E attendance																	2.59	1.27	5.25	0.01
phTest	0.19				0.57				0.35				0.42				0.35			

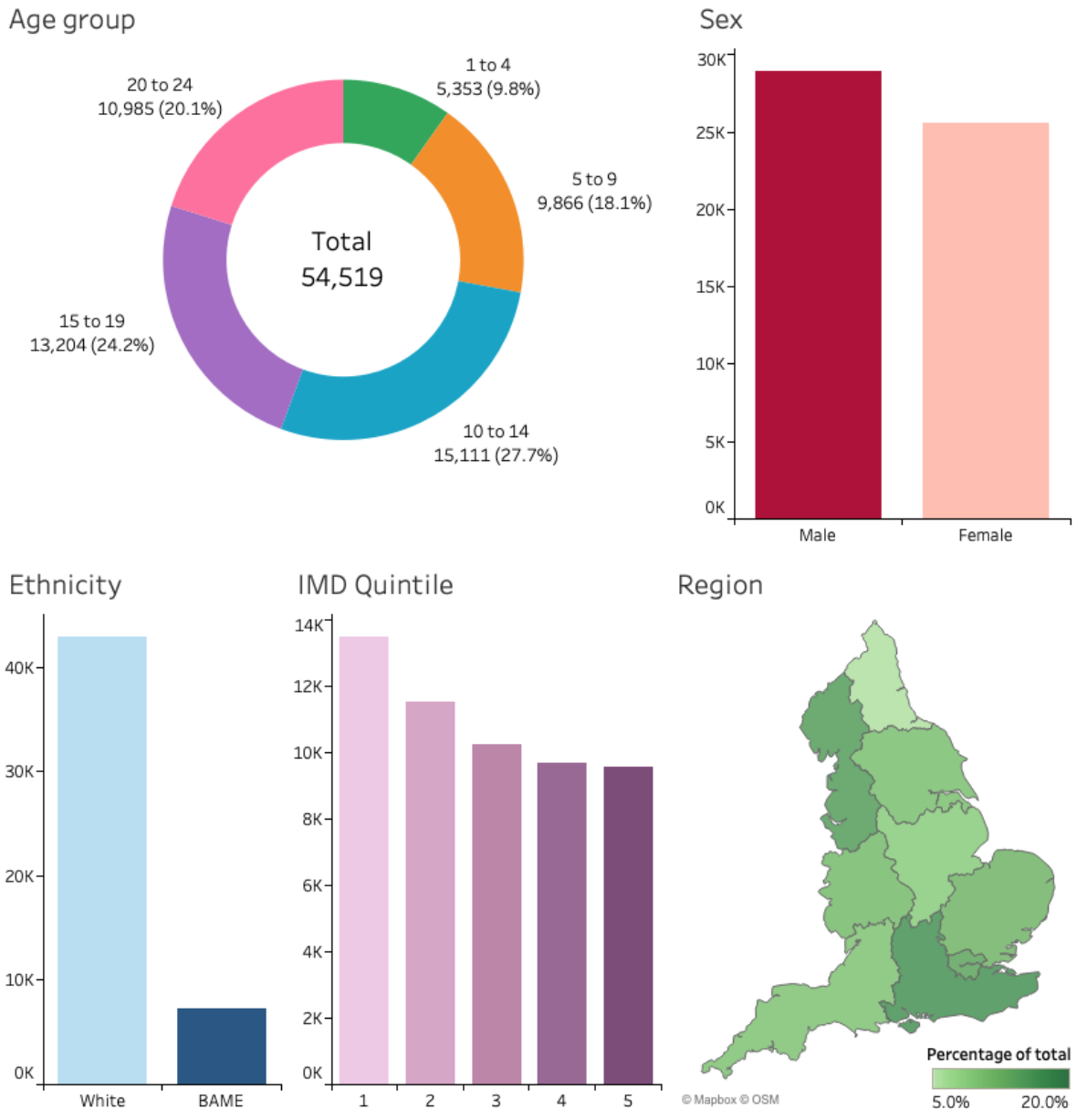
Table 40: (Continued) Cox regression output for hazard of death due to asthma following healthcare contacts and adjusted for background variables

	Not attending outpatients (excluding general appointments)				Transition (excluding general paediatrics)			
	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.91	0.82	1.01	0.08	1.15	0.79	1.66	0.47
Age in years	1.03	1.00	1.07	0.08	1.06	0.86	1.31	0.56
Female sex	1.50	0.93	2.42	0.10	2.87	0.59	14.01	0.19
IMD (Most deprived)								
2	0.57	0.29	1.10	0.09	0.29	0.03	2.52	0.26
3	1.03	0.57	1.88	0.92	0.37	0.04	3.20	0.37
4	0.70	0.33	1.48	0.35	0.46	0.05	3.92	0.47
5	0.38	0.13	1.07	0.07	0.48	0.06	4.19	0.51
Not attending op	1.30	0.78	2.15	0.32				
Transition					0.81	0.19	3.47	0.77
phTest	0.16				0.24			

Diabetes Mellitus

The diabetes cohort contained 54,519 participants, of whom 53.1% were male, and 78.7% were white (ethnicity was missing in 7.9% of participants). 27.7% were 10-14 years old at the index admissions, 24.2% were 15-19, 20.1 were 20-24, 18.1% were 5-9 and 9.8% were 1-4. 24.7% lived in the most deprived IMD quintile category, and 17.5% in the least deprived quintile category. The region with the most participants was the South East with 8733 (16.0% of the total), and the region with the least number of participants was the North East with 3026 (5.6% of the total) (figure 61)

Figure 61: Diabetes mellitus cohort visual summary of background characteristics



Description of the diabetes cohort

Within the diabetes cohort, there were 301 deaths (0.6%) and of these 143 (47.5%) were due to diabetes (table 34, p.240). Overall 5-year survival following the index admission was 99.4% for all causes of death, and 99.8% where diabetes was the primary cause of death. 37.5% of participants had least 2 further admissions with diabetes, with 10.1% having at least 5 further admissions. 94.7% had a planned specialist or general clinic planned, and of these 68.2% did not attend at least one outpatient appointment. 86.4% had a specialist clinic appointment, and of these 64.7% did not attend on at least one occasion. 11,037 participants transitioned to adult services (20.2%) when general paediatric clinics were included in this definition, and 7431 participants transitioned (13.6%) when general paediatric clinics were excluded from this definition. 30.2% of participants attended A&E on at least 2 occasions.

Diabetes cohort univariable analyses

Output from the univariable cox regression analysis is shown in table 41 (p.259). Within the diabetes cohort, index year was significantly associated with decreased hazard of death (HR 0.80 [0.74 – 0.86], p<0.001 for each additional year of entry to the study after 2007). Age in years was also associated with significantly higher hazard of death (HR 1.23 [1.18 – 1.29], p<0.001). Female sex was associated with significantly lower hazard of death (HR 0.64 [0.46 – 0.90, p=0.011). Participants living the 4th most deprived IMD quintile category had significantly lower hazard of death compared to those living in the most deprived quintile category (HR 0.47 [0.26 – 0.82], p=0.008).

In univariable analyses, healthcare activities which were significantly associated with hazard of death were: further admissions with diabetes (HR 4.46 [2.73 – 7.28], p<0.001 for 2-4 further admissions, HR 36.90 [22.15 – 61.48], p<0.001 for 5 or more further admissions); contact with mental health services (HR 2.71 [1.78 – 4.12], p<0.001); not attending at least one planned specialist or general clinic appointment (HR 3.48 [2.07 – 5.84], p<0.001); not attending a specialist appointment (HR 5.14 [2.95 – 8.96], p<0.001); and taking longer than 6 months to transition to adult services (including general paediatric appointments HR 2.53 [1.22 – 5.23], p=0.013; excluding general paediatric appointments HR 5.11 [1.74 – 15.01], p=0.003).

Diabetes cohort multivariable analyses

Table 42 (p.260) shows the output for assessing model fit for background variables for the diabetes cohort. Compared to a model only including the year of entry in to the study, the addition of age in years and then sex improved model fit (LRT p<0.001 and p=0.01 respectively). The LRT after the addition of IMD to this model approached significance (p=0.07). The addition of region to the model did not improve model fit, and was omitted. The final model used to adjust background characteristics of participants included year of index admission, age in years, sex and IMD quintile category (model D).

Healthcare contacts and hazard of death within the diabetes cohort

Table 43 (p.261) shows cox regression output for healthcare activity among the diabetes cohort after adjusting for year of index admission, age in years, sex and IMD. Hazard of death was significantly associated with further admissions with diabetes (2-4 further admissions HR 3.94 [2.40 – 6.47], p<0.001; 5 or more further admissions HR 26.51 [15.74 – 44.66], p<0.001); having any contact with mental health services (HR 2.75 [1.80 – 4.21], p<0.001); not attending a specialist outpatient appointment (HR 2.36 [1.32 – 4.23], p<0.001); taking longer than 6 months to transition to adult services (excluding general paediatric appointments) HR 3.06 [1.10 – 8.48], p=0.03). Taking longer than 6 months to transition was also associated with significantly increased mortality hazard when general paediatric appointments were included, but this was borderline (HR 2.09 [1.00 – 4.36], p=0.049). Results from the two sensitivity analyses (participants restricted to 10-24, and participants with no further healthcare episodes after the index admission excluded) were similar to the main analysis. The proportional hazards assumption was shown to be valid in all univariable and multivariable analyses undertaken (phtest p>=0.05).

Table 41: Univariable cox regression output for the diabetes cohort. Hazard of death due to diabetes by baseline characteristics and healthcare activity

	Diabetes Mellitus deaths				
	HR	lower	upper	p	PhTest p
Background variables					
Year of entry	0.80	0.74	0.86	<0.001	0.35
Age in years	1.23	1.18	1.29	<0.001	0.49
Female sex	0.64	0.46	0.90	0.011	0.12
IMD quintile (baseline most deprived)					
2	0.96	0.63	1.48	0.87	0.13
3	0.64	0.39	1.05	0.08	
4	0.47	0.26	0.82	0.008	
5	0.58	0.34	0.98	0.04	
English region (baseline North East)					
North West	0.90	0.39	2.05	0.80	0.69
Yorkshire and Humber	1.06	0.46	2.49	0.89	
East Midlands	1.25	0.54	2.93	0.60	
West Midlands	1.15	0.50	2.63	0.75	
East of England	1.02	0.44	2.37	0.96	
London	1.06	0.47	2.40	0.88	
South East	0.86	0.38	1.95	0.71	
South West	0.55	0.21	1.47	0.23	
BAME ethnicity	0.56	0.26	1.22	0.14	0.59
Healthcare contacts					
2 -4 further admissions	4.46	2.73	7.28	<0.001	0.37
5 or more further admissions	36.90	22.15	61.48	<0.001	
Mental health contact	2.71	1.78	4.12	<0.001	0.16
Not attending appointment	3.48	2.07	5.84	<0.001	0.29
Not attending appointment (excl general)	5.14	2.95	8.96	<0.001	0.46
More than 1 attendance to A&E	1.04	0.95	1.15	0.37	0.83
Transition > 6 months	2.53	1.22	5.23	0.013	0.20
Transition > 6 months (excl general)	5.11	1.74	15.01	0.003	0.25

Table 42: Model selection for time invariant predictors: Diabetes cohort (deaths due to diabetes)

	Model A				Model B				Model C				Model D				Model E			
	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.80	0.74	0.86	0.00	0.82	0.76	0.89	0.00	0.82	0.76	0.89	0.00	0.82	0.76	0.89	0.00	0.82	0.76	0.89	0.00
Age in years					1.23	1.18	1.28	0.00	1.23	1.17	1.28	0.00	1.22	1.17	1.28	0.00	1.22	1.17	1.28	0.00
Female sex									0.64	0.45	0.90	0.01	0.63	0.45	0.89	0.01	0.63	0.45	0.89	0.01
IMD (Most deprived)																				
2													0.98	0.64	1.51	0.94	0.97	0.63	1.51	0.91
3													0.67	0.40	1.10	0.11	0.66	0.40	1.11	0.12
4													0.51	0.29	0.91	0.02	0.50	0.28	0.90	0.02
5													0.67	0.39	1.13	0.13	0.65	0.37	1.13	0.13
Region (North East)																				
North West																	0.96	0.42	2.19	0.92
Yorkshire & Humber																	1.22	0.52	2.85	0.65
East Midlands																	1.50	0.64	3.51	0.35
West Midlands																	1.28	0.56	2.95	0.56
East England																	1.36	0.58	3.19	0.48
London																	1.21	0.53	2.73	0.65
South East																	1.18	0.51	2.73	0.70
South West																	0.73	0.27	1.96	0.53
AIC	2902.29				2791.65				2786.70				2785.93				2797.39			
BIC	2914.89				2816.86				2824.52				2874.17				2986.48			
PhTest p	0.35				0.54				0.26				0.12				0.29			
LRT p					0.00				0.01				0.07				0.81			

Table 43: Cox regression output for hazard of death due to diabetes following healthcare contacts and adjusted for background variables

	Mental Health				Further admissions				Not attending outpatients				Transition with general paediatrics				A&E attendances			
	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.82	0.76	0.89	<0.001	0.89	0.82	0.96	<0.001	0.78	0.71	0.86	<0.001	1.15	0.92	1.44	0.22	0.98	0.74	1.31	0.90
Age in years	1.22	1.17	1.28	<0.001	1.21	1.16	1.27	<0.001	1.22	1.16	1.29	<0.001	1.13	0.96	1.34	0.14	1.25	1.12	1.38	<0.001
Female sex	0.60	0.43	0.84	<0.001	0.48	0.34	0.68	<0.001	0.57	0.39	0.83	<0.001	0.57	0.28	1.16	0.12	0.58	0.24	1.44	0.24
IMD (Most deprived)																				
2	1.01	0.66	1.55	0.97	1.11	0.72	1.70	0.65	0.95	0.59	1.52	0.82	0.80	0.30	2.11	0.65	0.92	0.25	3.43	0.90
3	0.69	0.42	1.14	0.14	0.83	0.50	1.37	0.47	0.65	0.38	1.13	0.13	0.81	0.31	2.13	0.67	1.36	0.39	4.70	0.63
4	0.53	0.30	0.94	0.03	0.70	0.40	1.24	0.22	0.46	0.24	0.88	0.02	0.35	0.10	1.29	0.12	1.16	0.31	4.32	0.83
5	0.69	0.41	1.17	0.17	0.99	0.58	1.69	0.98	0.68	0.38	1.21	0.19	0.71	0.26	1.95	0.50	1.25	0.33	4.68	0.74
Mental Health	2.75	1.80	4.21	<0.001																
Further admissions																				
2-4					3.94	2.40	6.47	<0.001												
> = 5					26.51	15.74	44.66	<0.001												
Not attending op									1.53	0.90	2.58	0.11								
Transition													2.09	1.00	4.36	0.049				
A&E attendance																	1.14	0.33	3.86	0.84
phTest	0.09				0.06				0.25				0.21				0.70			

Table 43: (continued) Cox regression output for hazard of death due to diabetes following healthcare contact adjusted for background variables (ages 10-24 only)

	Not attending outpatients (excluding general appointments)				Transition (excluding general paediatrics)			
	HR	lower	upper	p	HR	lower	upper	p
Year of entry	0.80	0.71	0.89	<0.001	1.27	0.90	1.78	0.17
Age in years	1.20	1.12	1.27	<0.001	1.13	0.90	1.43	0.29
Female sex	0.45	0.29	0.69	<0.001	0.62	0.24	1.59	0.32
IMD (Most deprived)								
2	1.00	0.60	1.67	0.99	0.93	0.25	3.47	0.91
3	0.66	0.36	1.20	0.18	0.90	0.24	3.37	0.88
4	0.32	0.14	0.73	0.01	0.25	0.03	2.15	0.21
5	0.72	0.39	1.34	0.30	0.93	0.25	3.46	0.91
Not attending op	2.36	1.32	4.23	<0.001				
Transition					3.06	1.10	8.48	0.03
phTest	0.44				0.90			

Chapter 8 discussion

These population-level analyses of CYP survival after admission with epilepsy, asthma and diabetes, provide key insights in to identifying CYP at greatest risk of death.

Sociodemographic factors

Similar to previous chapters, I found significant variation in hazard of death by deprivation and geographic region, after adjusting for sex, age and index year. Within the epilepsy cohort, mortality hazard in the South of England was double that for the North East, and for diabetes and asthma, there were significant associations with reduced mortality hazard in less deprived CYP. Differences in mortality hazard by IMD category persisted even after the inclusion of certain healthcare activities within the asthma and diabetes cohorts. Less deprived CYP had significantly reduced mortality hazard after adjusting for all other factors including *not attending appointments* in both asthma and diabetes, and when *contact with mental health services* was included for CYP with diabetes. This again highlights pervasive associations of deprivation and mortality hazard for CYP. A key focus of efforts to improve mortality in these conditions should be to address the impact of these factors.

Healthcare factors

Recurrent admissions

After adjusting for age, sex, IMD quintile category and year of entry to the study, I found recurrent admission to hospital, and multiple attendances to A&E, to be associated with increased hazard of death in all cohorts examined. Explanations of recurrent admissions will differ between the three cohorts. For asthma and epilepsy, recurrent admissions may reflect more severe disease related to biological factors, poor chronic disease control, or both. With diabetes however, there is little clinical variation in insulin deficiency[309] and so recurrent admissions here represent a clearer signal of poor control in the community. In both cases however, these patterns should raise concerns that require further investigation.

Previous studies have shown a large proportion of emergency admissions in CYP are thought to be preventable, particularly for asthma and diabetes,[310] where I found the effect size to be greatest. Readmission to hospital has also been found to be associated with subsequent

death in diabetes, asthma and epilepsy, although much of this work is focused on adults.[273,311-314] Kao conducted a population level analysis in Taiwan and found increased hazard of death from all causes compared with matched controls after admission with DKA during 8 years of follow up, but this only included 230 patients aged 0-17.[311] Gibb found admission with Diabetic Ketoacidosis (DKA) among 628 adults to be associated with a 5.2% risk of death (follow up 4.1[2.8-6.0] years), rising to 23.4% in those with recurrent admissions (2.4[2.0 – 3.8] years of follow up).[312] Similar to these findings, I found the hazard of death to rapidly increase amongst CYP who are repeatedly admitted with diabetes, and the vast majority of these are due to DKA. However, I found the overall hazard to be much lower than reported by Gibb, with 5-year survival following the index admission of at least 99% in all age groups studied.

Fleming et al[313] examined risk of hospitalization and death amongst children on antiepileptic medication compared to those not amongst 766,244 children attending Scottish schools between 2009 and 2013. The authors found increased risk of hospitalization and death amongst CYP prescribed anticonvulsants, particularly in the first year after starting treatment, but did not examine how further admissions affect mortality risk.[313] Moss et al[314] studied long term mortality outcomes amongst 73,000 patients aged 16 and above admitted with seizures to Intensive Care in Scotland between 2005 – 2014. They found the hazard of death amongst those with seizures was 17% higher than those without, but again did not examine the effect of recurrent attendances or admissions.[314] Recurrent admissions with epilepsy are likely to indicate increased seizure activity, which is the main risk factor for Sudden Unexpected Death in Epilepsy (SUDEP),[315] has been associated with increased healthcare use and mortality in children with epilepsy.[316]

Similar to diabetes and epilepsy, admissions and recurrent attendances to A&E of CYP with asthma has been highlighted as indicating poor control and increased risk of death.[273] Reflecting this, one of the recommendations within the National Review of Asthma Deaths in 2014 was that CYP should be seen in secondary care after an admission or after two attendances to A&E within a year.[273] My findings support these concerns, with hazard of death more than 4 times higher amongst CYP who had at least 2 admissions during follow up. Most asthma deaths occur before reaching hospital,[273] and death during an admission has

previously been shown to be extremely rare – with only 7 deaths in 94,000 admissions of 0-16 year olds between 2000 – 2005 in one population level analysis in England.[317] The vast majority of CYP with asthma are managed exclusively in primary care, and most admissions are preventable.[310] In one recent study of 14,405 CYP identified as having asthma through GP records in North West London, only 5% were admitted during a 12 month period and 31 (<1%) had between 2 and 6 admissions.[318] Only CYP who had been admitted to hospital were included within the asthma cohort in my analysis, and so these CYP already represent higher risk group, although more than 70% then had no further admissions during follow up. Among these, CYP who then go on to be admitted on several occasions represent a particularly vulnerable cohort of CYP, who likely require additional support to manage symptoms in the community.

Missed appointments

Not being brought to an appointment was associated with increased hazard of death in all three cohorts, although associations differed between cohorts according to whether general clinics were included or not. Within the epilepsy cohort, removing general clinics made little difference to the results, with around a 30-40% increase hazard of death amongst CYP who missed an appointment compared with those who did not in both analyses. Amongst CYP with diabetes, I only found significant associations when general clinics were excluded, but the effect size was greater, with more than twice the hazard of death amongst CYP who missed an appointment. Within the asthma cohort, I only found significant associations when both general and specialist clinics were included, with around a 60% increase in hazard of death amongst those who missed an appointment.

Excluding general appointments increases the specificity of the cohorts, as CYP who attend general clinics may be doing so for other reasons other than the index cause. Although this allows us to be more confident regarding the nature of outpatient activity, it also decreases sensitivity, as appointments in general clinics for the management of asthma, epilepsy or diabetes will be missed. The effect of this varied between cohorts, reflecting differences between the conditions in terms of pathophysiology and the proportion of CYP who require tertiary input. Only around 20% of CYP with asthma had any planned appointment in a

specialist clinic, compared with more than 70% in CYP with epilepsy or diabetes, and so it is difficult to interpret results within the asthma cohort when general clinics were excluded. Previous work has also identified missed appointments being related to poor outcomes in CYP with chronic diseases, but I am not aware of population level analyses to examine associations with mortality risk. Missed appointments have been shown to be associated with increased unplanned healthcare care amongst children with neurodisability,[285] and a recent study also identified missed appointments as a common factor in a thematic analysis of 23 serious case reviews where there was a medical cause of death.[286] Not attending appointments was also proposed as a factor to consider when defining severe asthma in a recent *Lancet commission* on airway disease,[287] and as a concern within the National Review of Asthma Deaths in 2014.[273] Not attending appointments has previously been associated with deprivation and safeguarding concerns,[89] and the observed associations here may represent incomplete adjustment for these and other confounders. However, the aim of these analyses is to allow for CYP who are vulnerable to increased mortality hazard to be identified, rather than explain causation.

Planned contact with mental health services

I found CYP who had any planned contact with mental health services had more than double the mortality hazard over the follow up period within the diabetes cohort, but no significant associations in the other cohorts. Multiple previous studies have found increases in mental health problems among individuals with diabetes.[289,290] These associations are complex, and may be bidirectional; poor glycaemic control in the two years after diagnosis in adolescence is associated with later psychiatric comorbidity, and CYP with psychiatric disorders have worse disease control and increased rates of hospitalization due to DKA.[319,320] Young adults with diabetes and comorbid mental health problems have been shown to be at increased mortality risk.[289] This highlights the need to incorporate the need for screening of mental health problems within diabetes management, and Matlock et al. recently showed targeted mental health interventions can reduce suicidal ideation among adolescents with type 1 diabetes.[321] I did not find any association between planned mental health contact and mortality within the epilepsy cohort, contrary to multiple previous studies finding strong associations with mental health and epilepsy.[293] This may be explained by unmet mental health need in CYP with epilepsy, and concerns have been raised regarding barriers to access

to mental health services in this group.[322] Other explanations include poor identification of cases who have been referred to mental health services, as I was only unable to capture community CAMHS services in these analyses. Further, I only modelled mortality due to each chronic condition, and so will not have captured deaths due to self-harm associated with psychiatric illness.

Transition to adult services

CYP within the diabetes and epilepsy cohorts who took longer than 6 months to transition to adult services were found to have between 2-3 fold increased hazard of death compared to those who took less than six months. Other studies have established transition to adult care can be associated with poor health outcomes in young people with epilepsy and diabetes,[298,301,303] but I am not aware of analyses exploring associations with mortality. However, previous work has found transition to adult services to be associated with increased mortality risk amongst young people with HIV and sickle cell disease.[299,300,323,324] Foster et. al. examined clinical outcomes among young people with perinatally acquired HIV as they transition to adult care within a specialised adolescent service in the UK.[299] Within a cohort of 180, mortality in the years immediately post transition to adult services was found to be 10 times higher than the adult population 19-29.[299] A similar sharp rise in mortality was found within a cohort of 725 young adults living with HIV in New York in the year after they transitioned to adult services.[300] Others have noted a sharp rise in mortality amongst young people with sickle cell disease in the years immediately after transition to adult services.[323,324] However, these studies did not assess how an indicator for *quality* of transition may be associated with mortality risk, only that transition itself is associated with increased vulnerability.

Strengths and weaknesses

Strengths of these analyses include the near national coverage of CYP admissions to secondary care for key chronic conditions provided within HES, up to 10 years of follow up time, and being able to link patients across different types of healthcare activity. However, these analyses have a number of limitations. It is important to view increased hazard ratios described here within the wider context of background mortality risk, as deaths within in each

cohort were extremely rare. There are important questions around HES data reliability, which varies over time, region, and dataset, as described in Chapter 2. The scale of these data is both a strength and a concern, as different data cleaning and management decisions may have large impacts on these results. As with population level trends in admission described in Chapter 7, I have only used primary reason for admission to define each cohort, and have not attempted to examine how CYP with comorbidities may be at increased mortality risk. Some CYP may have had asthma, diabetes or epilepsy recorded only as a secondary diagnosis across all admissions, and so I will not have identified them in these data. I have also not explored how different types of healthcare activity I analysed correlate with one another. We could expect that CYP who miss appointments are also more likely to disengage during transition to adult services, have poor disease control in the community requiring admissions and A&E attendances, and other mental health comorbidities. However, the aim of these analyses is not to ascribe causation, only to identify CYP at most risk of death through associations with both background characteristics and healthcare activity.

Further analyses are required which expand on the derived variables I have used to define healthcare activity. I created a dichotomous variable to identify CYP who ever missed a planned appointment, and did not explore increased mortality hazard within those who repeatedly were not brought to outpatients. Within mental health, I was only able to identify planned outpatient mental health services within an NHS Hospital, or emergency admissions, and so did not capture much of Child and Adolescent Mental Health Services (CAMHS) which occur in community NHS trusts not present in my data. To fully understand the burden of mental health comorbidity in CYP admitted with these chronic conditions, and how this is associated with mortality hazard, linking other data including the NHS Digital Mental Health Services Dataset is required. Within transition, as data were only available up to 24 years, I could not reliably identify CYP who failed to transition, and therefore likely represent the most-high risk group. I defined timely transition as occurring within 6 months of leaving paediatric services, and although this may be appropriate for conditions with frequent outpatient appointment such as diabetes, for other conditions different definitions may be more informative. I also did not assess the other important aspects of transition, although defining successful transition itself is complex.[325] Future analyses should include exploring factors associated with poor transition in greater detail, including the age at which transition

occurs within diabetes and epilepsy, as there is some evidence that later age of transition is associated with better health outcomes.[326,327]

Potential policy responses

Explanations for associations I present here between sociodemographic factors, patterns of healthcare activity and subsequent mortality hazard are complex, and relate to multiple interacting determinants of health. Broadly, these analyses can be used to identify patterns of activity which should raise concerns regarding increased vulnerability of CYP. They also quantify increase in mortality hazard associated with activity known to be of concern, for example not attending appointments and recurrent attendances to secondary care. These estimates may be used to highlight the need for further investigation to understand these patterns of healthcare activity in CYP, and so inform interventions to reduce individual mortality risk.

Health care activity I identify as being associated with increased mortality provide examples where better integration across horizonal, vertical, longitudinal and population domains may prevent deaths.[66] Improved co-ordination between secondary and primary care, and within mental health services, may facilitate identifying that CYP who may be at additional risk when they present to different parts of the health service. Notably, better integration and communication between parts of the health service has been highlighted contributory factors in preventable deaths due to asthma at individual case review,[272] and within potential policy interventions to improve mortality in England due to other causes.[45] Understanding why CYP are not brought to appointments requires exchange of information between secondary and primary care, but also across sectors such as education and social services. Finally, the associations I describe between length of time between last paediatric appointment and first adult appointment and mortality reflect the importance of longitudinal integration of services, and co-ordination between teams working within the same service.

Conclusions

These findings show how recurrent admissions, mental health contact, difficulties with transition, and missed appointment are associated with increased mortality hazard. Being

able to quantify these associations may support clinicians in counselling CYP and their families after admission with these chronic conditions, identify CYP who are at most at risk, and highlight the potential need for further support.

Chapter 9

UK trends in mortality in young people 10-24 in the global context

Analyses in this thesis have highlighted concerns around mortality in young people 10-24 in the UK. I have shown that reductions in UK mortality in this age group have been slower than younger children, driven by poor progress in improving outcomes for predominant causes of death in young people. Although the UK continues to perform well for injury mortality in 10-24, mortality is significantly higher than the EU15+ for important non-communicable diseases (NCD) such as epilepsy, asthma and diabetes. Amongst 1-24, adolescents and young adults have some of the widest variation in mortality within the UK, driven by high mortality due to injury, self-harm and drug disorders in Scotland and Northern Ireland, and there are also steep social gradients in outcomes in this age group. In chapter 8 I found important opportunities to identify CYP who may be at increased risk of death in the way health services are used, including transition from paediatric to adult services, and having contact with mental health services, both highly relevant to 10-24 year olds.

Concerns around UK mortality for 10-24 may reflect broader global trends in health outcomes for young people. Despite wider recognition of the importance of adolescent health to global development,[4,41,328-331] there is also growing concern that global adolescent health priorities continue to be neglected.[332,333] Global progress to improve health outcomes for young people has been slow, and major challenges remain in addressing social determinants of adolescent health and mortality, particularly in low and middle income settings, such as unmet contraception need, child marriage and access to quality secondary education.[332] Further, the COVID-19 pandemic continues to have far reaching consequences on the health of young people which are not fully understood. Although case fatality and morbidity due to COVID-19 in young people has been lower than in older adults,[334] this age group are particularly vulnerable to indirect effects of the pandemic, with ongoing disruption to education and employment likely to further hinder progress in health.[335]

Earlier work illustrated that global adolescent mortality was greater than previously recognised,[336] and that improvements have lagged behind those seen in younger children,[337]

(similar to my findings for the UK), despite a high proportion of adolescent deaths being from preventable causes.[338] Not only is mortality a fundamental indicator of health of young people,[120] but also serves as a provide a proxy for broader health outcomes in settings lacking high quality data.[339,340] As such, mortality is included in the indicator set for monitoring future progress in adolescent health. All-cause mortality amongst 10-19 is an indicator within the Global Strategy for Women's, Children's and Adolescent Health 2016-2030[4,5], and Sustainable Development Goal (SDG) 3 includes indicators for causes of death which are highly relevant to young people including maternal mortality (SDG indicator 3.1.1), suicide mortality (3.4.2) and deaths due to road traffic injury (3.6.1).[341]

Previous studies of global adolescent mortality

I undertook a literature review using PubMed and EMBASE to understand the extent of previous work on global trends in adolescent mortality, and identify possible gaps in this evidence base. For this I included the following search terms in titles or abstracts: ("adolescent" OR "young people" AND ("trends" OR "patterns") AND ("death" OR "mortality") AND ("world" OR "global" OR "international.") After removing duplicates, I reviewed the titles and relevant abstracts of 3,503 studies. I only found one study which focused on global mortality patterns in adolescents (10-24), published in 2009.[336] Using data from 2004, Patton et al. demonstrated the considerable burden of global adolescent mortality, and analysed geographic variation in outcomes, but did not explore trends over time.[336] Two further studies reported trends in global mortality or years of life lost (YLL) in adolescents and young people from 1990. As part of wider analyses of patterns of disease and risk factors in 10-24, these studies found considerable variation in improvements in mortality and YLL by country, age group and sex.[332,338] Other studies I identified which examined adolescent deaths either included only 10-14 or 10-19 year olds, focused on one region or group of countries, or were part of a study of mortality in other age groups.

Since publication of Patton et. al's analysis of global mortality in young people in 2009[336] there have been huge changes to patterns of health risk, population growth, and improvements in the availability and quality of mortality estimates in this age group. The impact of these changes on global mortality in 10-24 has not been previously been described.

Agencies providing adolescent mortality estimates for a broad range of countries include the United Nations Population Division, Department of Economic and Social Affairs (UNDOP),[342] the World Health Organization (WHO),[343] US Census Bureau,[344] and the United Nations Inter-agency Group for Child Mortality Estimation.[345] However, as described in Chapter 2, the great strength of the Global Burden of Disease (GBD) study is that it provides annually updated, age specific mortality estimates (including uncertainty intervals) covering almost all countries and territories in the world.[120] Further, the availability of estimates in GBD 2019 of all-cause mortality from 1950 and cause specific estimates from 1980[120] provides a unique opportunity to analyse long-run trends over time, and so identify both successes and areas requiring global and national investment.

Here I use GBD 2019 estimates[120] to analyse current and long term trends in mortality in 10-24 globally and in 204 countries and territories. I use this age range to capture the social, biological and neurocognitive transitions that occur during this stage of the life course,[94] and use the terms “adolescent” and “young person” synonymously.

Work presented in this chapter has been completed in close collaboration with the Institute of Health Metrics and Evaluation (IHME), and the Murdoch Children’s Research Institute (MCRI), University of Melbourne, where I worked as a visiting academic as part of an MRC Fellowship from Feb – April 2019. In addition to my primary and secondary supervisors, I would like to acknowledge specific contributions for this chapter from George Patton, Pete Azzopardi, Kate Francis and Susan Sawyer (MCRI), and Ali Mokdad, Simon Hay and others within the GBD Collaborator Network (IHME).

Related publication (under review):

Ward JL, Azzopardi P, Francis K, Santelli J, Skirbekk V, Sawyer S, Mokdad A, Kassebaum N, Hay S, Patton G, Viner R, GBD Collaborators. Global, regional, and national mortality among young people aged 10 to 24 years, 1950-2019: a systematic analysis for the Global Burden of Disease Study 2019

Chapter 9 methods

Data

For this analysis I used data provided by the Institute for Health Metrics and Evaluation (IHME) Global Burden of Disease study 2019 (GBD 2019).[120] Details of the GBD study are described in Chapter 2. Estimates were available for number of deaths, years of life lost (YLL) and mortality rate per 100 000 population with uncertainty intervals (UI) by sex and age group in 204 countries and territories. Mortality estimates for all-causes were available from 1950-2019, and by cause of death from 1980-2019.

I used methods described in Chapter 3 to group cause of death. Broadly, I used data at level 2 of the GBD mortality hierarchy, but modified this to account for leading causes of death in 10-24 year olds which require distinct policy responses. Firstly, I analysed *self-harm* (i.e. suicide) separately from other causes within the level 2 group *self-harm and interpersonal violence*, which I subsequently refer to as *interpersonal violence and conflict*. Secondly, due to the importance of maternal deaths in this age group, I separated the level 2 group *maternal and neonatal disorders* into its two level 3 causes: *maternal disorders* and *neonatal disorders*.

The GBD 2019 mortality estimates were available for 204 countries and territories, (hereafter referred to as "countries"). This includes all members and associate members of the WHO. Estimates were also available for 21 GBD regions and 7 GBD super-regions (defined by both geography and income status). Here I primarily report outcomes by GBD super-region, with country and region level estimates available in supplementary material 3 part b and c. The 7 GBD super regions are: Central Europe, Eastern Europe and Central Asia; Latin America and the Caribbean; Southeast Asia, East Asia and Oceania; North Africa and the Middle East; South Asia; sub-Saharan Africa; High Income. Note that separate from the High Income GBD super-region, there are countries defined as high income by the World Bank in all other GBD super regions except sub-Saharan Africa and South Asia. However, when I discuss "High Income Countries" in this analysis I am referring to the GBD High Income super-region. The list of countries included in the analysis, their GBD region, GBD super-region and World Bank income classification for 2021 is found in the supplementary material 3 part a (table S1).

Analyses

I first describe current and long-term trends in all-cause mortality rate and number of deaths from 1950-2019, and by cause of death from 1980-2019, amongst 10-14, 15-19 and 20-24 by sex. I analyse relative risk for mortality between age groups by dividing the mortality rate in 20-24 and 15-19 by the mortality rate in 10-14 year olds. I analyse variation in outcomes by sex by calculating the ratio of male to female all-cause mortality rate. I analyse between country variation by calculating the ratio for all-cause mortality rate in 10-24 year olds in the highest to lowest decile country globally (90^{th} to 10^{th} centile), to account for extreme values in some location-years.

I then analyse the relationship between mortality rate per 100,000 in 10-24 year olds in 2019 and country development status using the GBD Socio-Demographic Index (SDI).[1] The SDI is a summary indicator of social and economic conditions that are strongly correlated with health outcomes. It is calculated from first determining a 0-1 index value for three components: average national educational attainment in those aged over 15, total fertility rate under 25, and lag-distributed income per capita, using the observed minima and maxima over the estimation period for each component to set the scales. The composite SDI is the geometric mean of these indices for each location-year.[1] I analyse the strength of the association between SDI and all-cause mortality rate per 100,000 in 10-24 year olds using Spearman's correlation coefficients. I then identified countries with lower or higher mortality in 10-24 year olds relative to their level of development. I did this using data provided by IHME derived as follows: first the expected value of years of life lost (YLL) by age group and sex was calculated based solely SDI for that location-year using a generalised additive model with a Loess smoother on SDI.[1] IHME then calculated the ratio of observed YLL to the expected value according to country SDI. The YLL are calculated as the sum of each death multiplied by the standard life expectancy at each age using GBD's standard life table. Note these data were only available from 1990–2017.

Finally, I assess variation in progress to reduce mortality across the early life course, comparing trends and current mortality burden in young people with infants, 1-4 and 5-9 year olds. I first report annual rates of change (1990 – 2019) for all-cause mortality rate for each

country by 5-year age group in 0-24 year olds. I did this using the β coefficient from linear regression models of mortality rate per 100 000 population against time for each country to estimate annual rate of change (expressed as a percentage). I used these models rather than estimates at the start and end of each time period to account for large fluctuations in country mortality due to war or natural disasters. I then identified countries with large differences in mortality performance by age group. I did this by comparing country-level all-cause mortality percentile in adolescents with that seen in children under 5, as this age group has been the focus of global programming and has experienced good mortality declines in recent years. Finally, I describe how the proportion of deaths in 0-24 which occur in 10-24 year olds has changed between 1950 and 2019., similar to methods used for the UK in Chapter 3. All analyses were performed in Stata 16 (StataCorp, College Station TX).

Chapter 9 results

Global mortality in young people 10-24 in 2019

Table 44 (p.279) shows the number of global deaths and mortality rate per 100 000 in 2019 and by GBD super-region for 10-24 year olds by sex, with data for 10-14, 15-19 and 20-24 in supplementary material 3 part a (tables S3-S5). Country level estimates are available in supplementary material 3 part c.

Within a total population of 1.86 billion people aged 10-24 in 2019, there were around 1.49 million deaths [95% uncertainty interval 1.39 – 1.59]. Just under half of these deaths occurred in 20-24 (692 000 [645 000 – 738 000]), with a third in 15-19 (499 000 [465 000 – 536 000) and a fifth in 10-14 (299 000 [276 000 – 325 000]. 61.0% of all deaths in 10-24 year olds occurred in males (910 000 [847 000 – 974 000]), with this proportion increasing with age (56.9% in 10-14; 60.5% 15-19; 63.2% 20-24). The greatest number of adolescent deaths occurred in South Asia in both sexes. Central Europe, Eastern Europe and Central Asia had the lowest number of adolescent deaths in both sexes. Mortality rates in 2019 increased with age across adolescence in all regions of the world, particularly in males, but with considerable variation. Within GBD super-regions, the relative risk of mortality in young adulthood (20-24) compared with early adolescence (10-14) ranged from 6.6 in the High Income GBD super-region amongst males, to 1.9 in North Africa and Middle East among females.

The mortality rate in 2019 in 10-14 ranged from 7.32 [6.90 – 7.78] in Denmark to 187.25 [165.74 – 217.44]] in Central African Republic amongst males, and from 6.01 [5.79 – 6.25] in Denmark to 115.73 [107.50 – 129.23] in Central African Republic amongst females. In 15-19 this ranged from 22.55 [21.50 – 23.72] in Denmark to 370.28 [305.42 – 448.95] in Lesotho amongst males, and 12.15 [12.02 – 12.29] in Japan to 248.02 [169.99 – 348.35] in Lesotho in females. In 20-24 the range was 36.24 [35.48 – 37.05] in Singapore to 559.77 [434.53 – 670.69] in Lesotho in males and 14.44 [14.05 – 14.85] in Singapore to 445.22 [303.38 – 636.53] in Lesotho in females.

Globally, 32.7% of deaths in 10-24 year olds in 2019 were due to transport injuries, unintentional injuries or interpersonal violence/conflict, 32.1% were due to communicable,

nutritional or maternal causes, 27.0% were due to non-communicable diseases (NCD) and 8.2% were due to self-harm. However, there was large variation in the leading causes of adolescent death by GBD super-region, sex and age. Amongst adolescent males, the leading cause of death in 10-14 was unintentional injury in all GBD super-regions except High Income countries, where neoplasms were the leading cause, and South Asia and Sub-Saharan Africa, where this was enteric infections. In males 15-24, the leading causes of death were transport injury in all GBD super-regions except Latin America and the Caribbean, where the leading cause was interpersonal violence and conflict, and Central Europe, Eastern Europe and Central Asia, where this was death due to self-harm.

Amongst adolescent females, the leading causes of death in 10-14 were neoplasms (Latin America and the Caribbean, Central Europe, Eastern Europe and Central Asia and High Income countries), unintentional injury (Southeast Asia, East Asia and Oceania), enteric infections (South Asia) and transport injuries (North Africa and Middle East). Amongst 15-19 the leading causes of death were transport injuries (High Income, North Africa and Middle East and Southeast Asia, East Asia and Oceania), self-harm (South Asia and Central Europe, Eastern Europe and Central Asia), interpersonal violence and conflict (Latin America and the Caribbean). Amongst 20-24 the leading causes of death were transport injuries (High Income), neoplasms (Southeast Asia, East Asia and Oceania and Central Europe, Eastern Europe and Central Asia), interpersonal violence and conflict (Latin America and the Caribbean) and cardiovascular diseases (North Africa and Middle East), self-harm (South Asia). HIV/AIDS and STI (sexually transmitted infections) was the leading cause of death in sub-Saharan Africa amongst females in all adolescent age groups 10-24. Although not the leading cause in any GBD super region, maternal deaths were still in the top three causes in 20-24 year old females in sub-Saharan Africa, North Africa and the Middle East, and South Asia, and were 4th highest in Latin America and the Caribbean.

Table 44: Global number of deaths and all-cause mortality rate per 100,00 in 10-24 by sex in 2019

	Number of deaths			Rate per 100,000	
10 to 24	Estimate	Uncertainty Interval	Percent of global total	Estimate	Uncertainty Interval
Males					
Global	909,678	[846,675 - 974,477]		95.41	[88.80 - 102.20]
Central Europe, Eastern Europe, and Central Asia	31,263	[28,845 - 33,776]	3.4	83.56	[77.10 - 90.28]
High-income	48,600	[48,045 - 49,176]	5.3	49.85	[49.28 - 50.44]
Latin America and Caribbean	96,676	[87,477 - 107,076]	10.6	130.62	[118.19 - 144.67]
North Africa and Middle East	73,335	[64,813 - 83,549]	8.1	88.07	[77.84 - 100.34]
South Asia	253,999	[224,664 - 286,215]	27.9	93.64	[82.82 - 105.51]
Southeast Asia, East Asia, and Oceania	157,271	[141,742 - 173,199]	17.3	73.31	[66.07 - 80.74]
Sub-Saharan Africa	248,533	[220,401 - 279,643]	27.3	141.60	[125.57 - 159.32]
Females					
Global	581,311	[531,162 - 634,825]		63.99	[58.47 - 69.88]
Central Europe, Eastern Europe, and Central Asia	13,032	[12,042 - 14,207]	2.2	36.70	[33.92 - 40.01]
High-income	19,715	[19,532 - 19,913]	3.4	21.28	[21.09 - 21.50]
Latin America and Caribbean	33,376	[29,924 - 37,078]	5.7	46.19	[41.41 - 51.31]
North Africa and Middle East	38,862	[34,148 - 45,205]	6.7	49.81	[43.77 - 57.95]
South Asia	224,137	[196,768 - 253,694]	38.6	88.05	[77.30 - 99.67]
Southeast Asia, East Asia, and Oceania	68,295	[61,737 - 75,149]	11.7	34.82	[31.47 - 38.31]
Sub-Saharan Africa	183,893	[159,437 - 213,930]	31.6	102.57	[88.93 - 119.33]

Trends in global mortality in young people 10-24 1950-2019

Annual global numbers of deaths in 10-24 year olds reduced by 21.7% from 1950 – 2019 (figure 62, p.282) during which time the world population in this age group has increased by 157% (see supplementary material 3 part a, figure S2). The majority of this decline was after 2000, with little change globally before that. The greatest declines in deaths have occurred in females, with a 30.0% decrease since 1950, compared with a decline of 15.3% in males, despite similar population growth (154% and 161% respectively). There were also large differences in trends in deaths by age group; deaths in 10-14 have declined by 37.5% in males and 37.9% in females; those in 15-19 declined by 17.8% in males and 27.9% in females; those in 20-24 have declined by 26.9% in females, and have *increased* by 0.8% in males.

In 10-14 the number of deaths has decreased in all GBD super-regions since 1950 except sub-Saharan Africa, where numbers have increased by 140.6% in males and 144.3% in females. The greatest declines in deaths since 1950 in 10-14 were in High Income countries (86.0% reduction in males and 87.3% reduction in females). In 15-24 males, the number of deaths has increased in all GBD super groups except High Income, Central Europe, Eastern Europe and Central Asia and Southeast Asia, East Asia and Oceania. The greatest increases in deaths in 15-24 males were in sub-Saharan Africa, where deaths increased by 180.5% in 15-19 and 218.2% in 20-24. The greatest decline in deaths in 15-24 males was in the High Income GBD super region, where deaths decreased by 72.6% in 15-19 and 66.0% in 20-24. In 15-24 females, deaths have decreased in all GBD super regions except North Africa and Middle East and sub-Saharan Africa. The greatest increase in deaths in 15-24 females was in sub-Saharan Africa in both 15-19 (175.7% increase) and 20-24 (164.3% increase). The greatest declines in deaths in 15-24 females were in High Income countries for both 15-19 (81.0% decline) and 20-24 (79.9% decline).

Figure 63 (p.283) shows mortality rate per 100 000 in 10-14, 15-19 and 20-24 year olds by sex and GBD super-region between 1950 and 2019. Amongst 10-14, global mortality rates reduced by 74.6% amongst males and 74.3% amongst females, with the greatest relative change in mortality in High Income countries (reductions of 88.2% in males and 89.0% in females). The GBD super-region with the smallest relative change in mortality rate was sub-

Saharan Africa, with reductions of 65.4% in males and 63.9% in females. All other regions achieved between a 72 and 88% reduction in mortality rate over this period in 10-14 in males and females.

Amongst 15-19, global mortality rate declines were 68.7% in males and 71.7% in females. The region with the greatest relative reduction in mortality in this age group was Southeast Asia, East Asia and Oceania, where the mortality rate declined by 80.1% in males and 86.1% in females. The region with the lowest relative reduction in mortality rate was sub-Saharan Africa for both sexes, with relative declines of 57.8% in males and 59.4% in females.

Amongst 20-24, global mortality rates reduced by 63.4% in males and 72.7% in females between 1950 and 2019. Relative declines in mortality were greatest in Southeast Asia, East Asia and Oceania for both sexes, reducing by 77.7% in males and 86.4% in females. Amongst males 20-24, the lowest relative decline was in Central and Eastern Europe and Central Asia, where mortality rates reduced by 46.1% since 1950. Among females 20-24, the lowest relative reduction in mortality was seen in sub-Saharan Africa, where mortality rates have declined by 60.7%.

The ratio of male to female mortality rate in 2019 was 1.2 for 10-14 year olds, 1.5 for 15-19 year olds and 1.7 for 20-24 year olds (see supplementary material 3 part a, figure S20). Mortality rate per 100,000 in 10-24 year olds was higher in males in all regions of the world except South Asia, where outcomes were similar. Sex differences in mortality were greatest in Latin America and the Caribbean in 20-24 year olds, where the mortality rate per 100,000 in males was more than three times that of females. The ratio of male to female mortality rate has been generally increasing for older adolescents (15-24) in all GBD super-regions between 1950 and 2019 except High Income and Central Europe, East Europe and Central Asia, where it has been reducing since the mid-1990s.

Figure 62: Global number of deaths in 10-14, 15-19 and 20-24 year olds from 1950 – 2019 by sex.

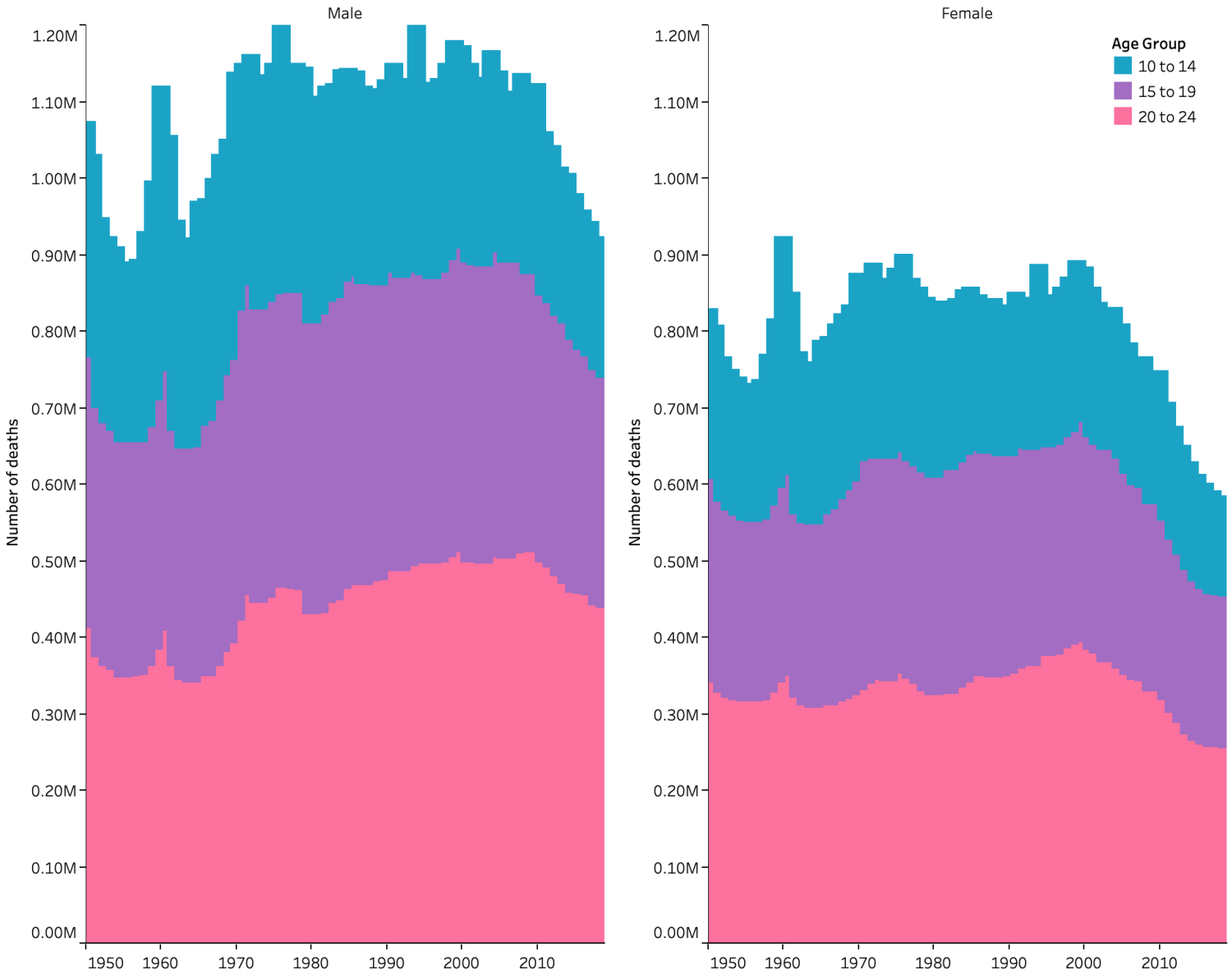


Figure 63: Mortality rate per 100,000 in 10-14, 15-19 and 20-24 year olds by sex and GBD super region between 1950 and 2019

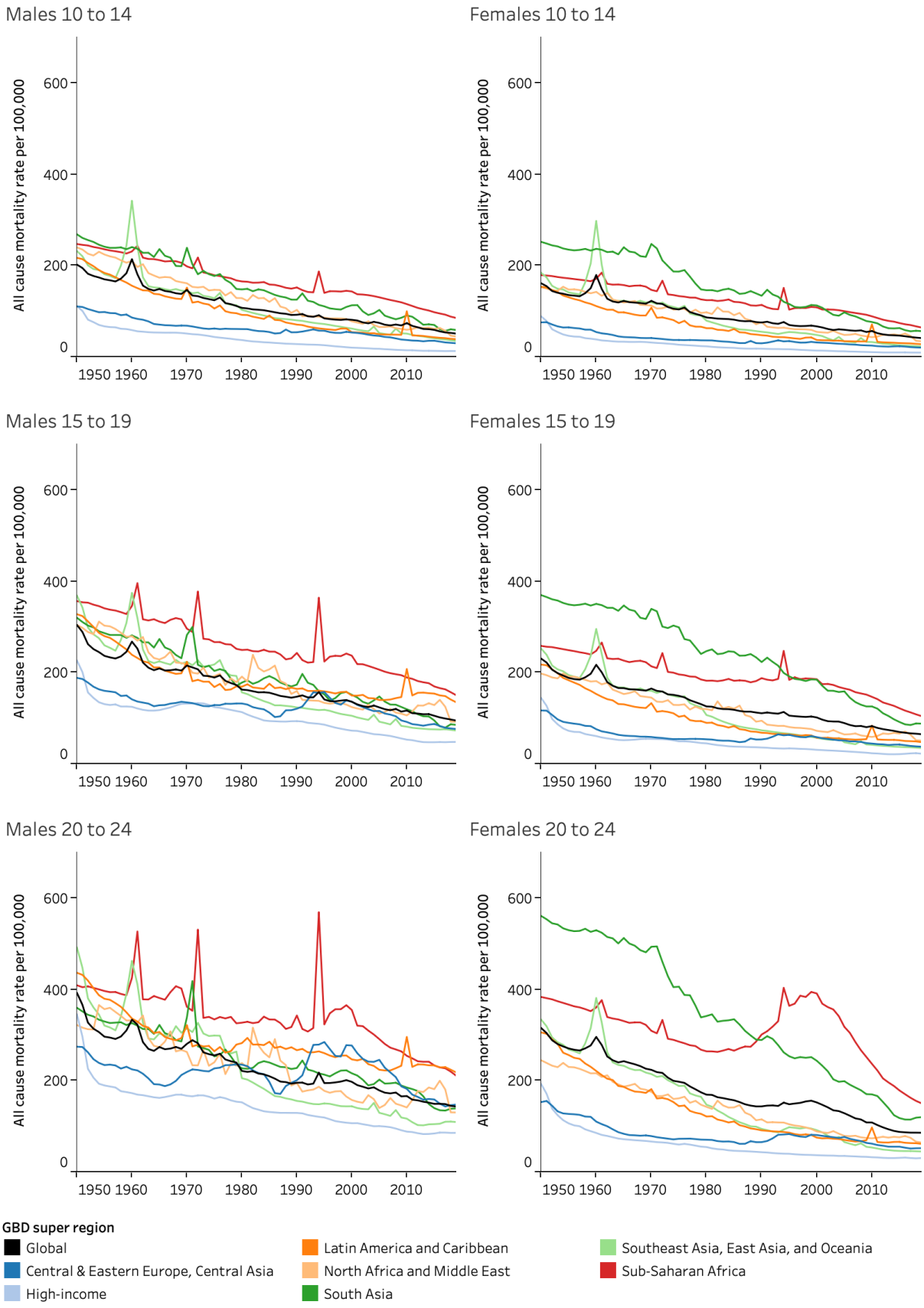


Figure 64: Ratio of mortality rate per 100,000 in the 90th centile to 10th centile country in 10-14, 15-19 and 20-24 year olds by sex between 1950 and 2019

Figure 65A: Percentage of total deaths by cause group in 15-19 year old males 1980 – 2019

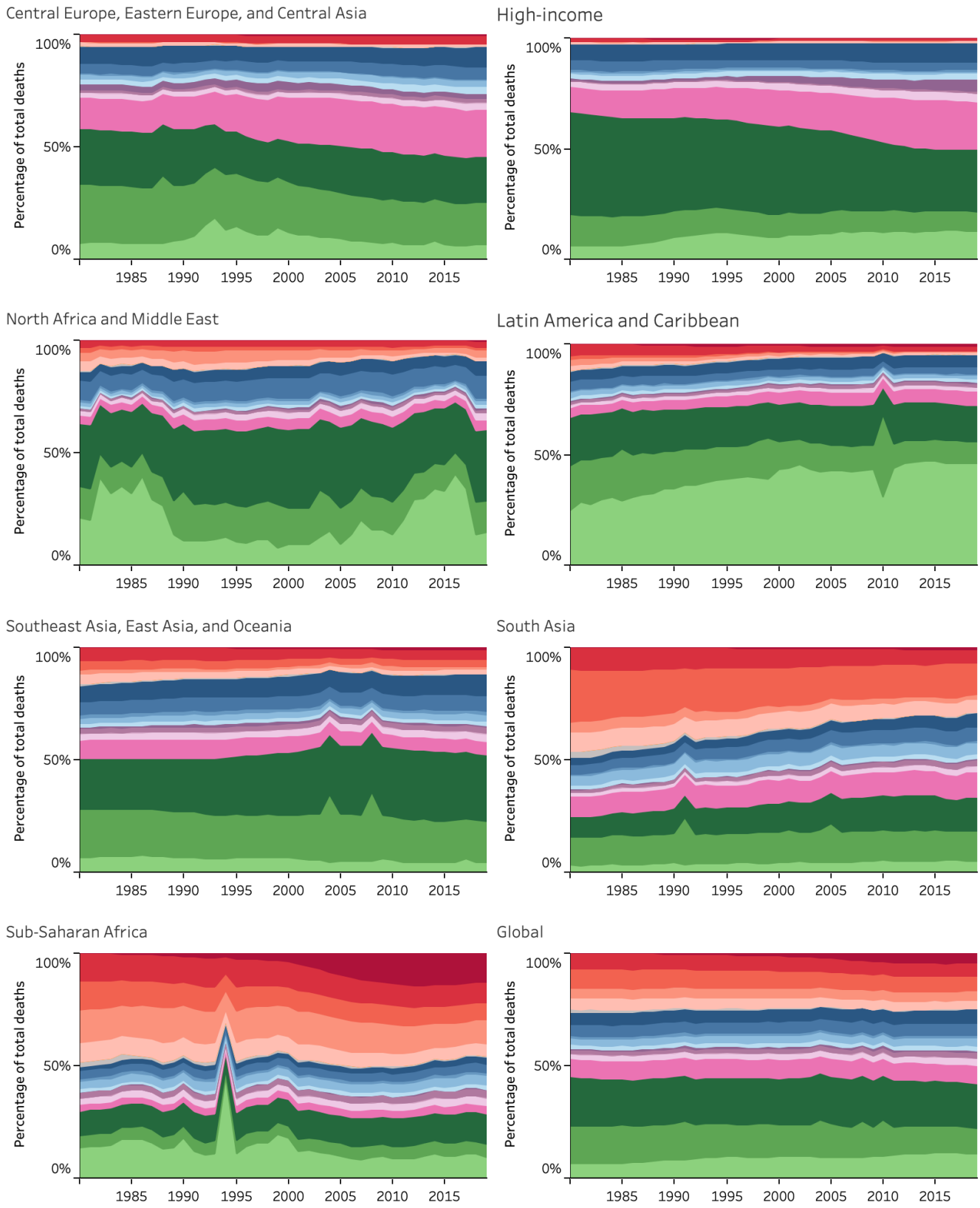
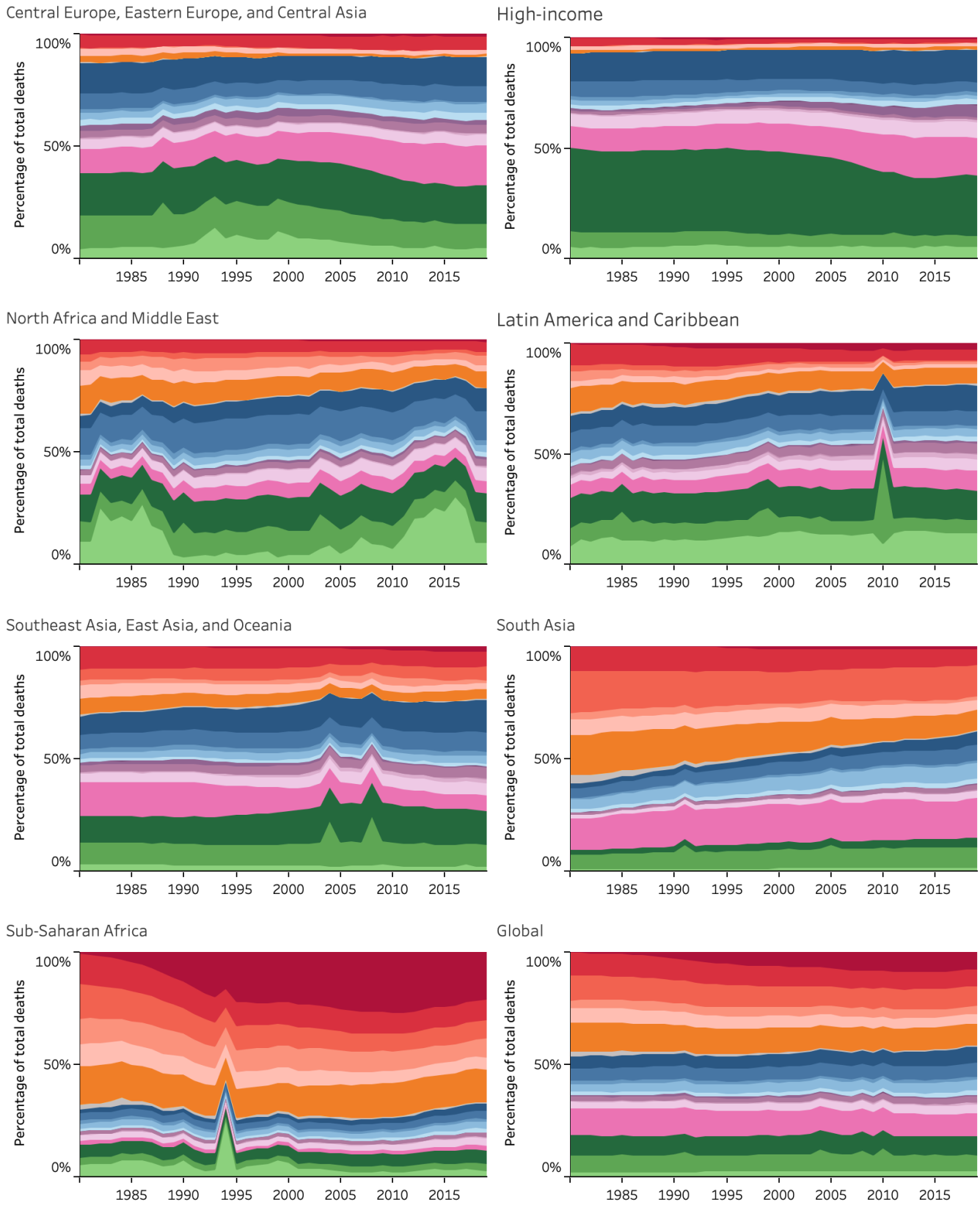


Figure 65B: Percentage of total deaths by cause group in 15-19 year old females 1980 – 2019



Inequality in mortality rate between countries was reported using the ratio of mortality rate for the highest decile country (90th centile) to lowest decile country (10th centile) in each year. In 2019 variations in mortality by country were greatest in 10-14 year olds, with the mortality rate in the 90th centile country around 9 times higher than that in the 10th centile country for both males and females. Inequality in outcomes by country has also increased over time for all age groups since 1950, although this appears to have fallen for 20-24 females since around 2000 (figure 64, p.284).

The percentage of total deaths by cause group from 1980 – 2019 in 15-19 year olds in each GBD super-region is shown in figure 65 A and B (p. 285) with equivalent figures for 10-14 and 20-24, and bump charts ranking cause of death between 1980-2019 for each age group, sex and GBD super-region, shown in supplementary material 3 part a (figures S50 – S112).

Reflecting the epidemiological transition, there have been large reductions in the importance of communicable and maternal causes to total adolescent deaths between 1980-2019 in Latin America and the Caribbean, South Asia, Southeast Asia, East Asia and the Caribbean and North Africa and the Middle East. Further, although maternal deaths still contribute a substantial proportion of global deaths in 20-24, this has fallen substantially over the study period. In Southeast Asia, East Asia and Oceania, North Africa and the Middle East, and Central Europe, Eastern Europe and Central Asia, maternal deaths have halved as a proportion of total deaths between 1980-2019, with large reductions also seen in South Asia and Latin America and the Caribbean. However, in sub-Saharan Africa, all of the top five causes of death in 2019 were communicable or maternal causes in 10-24 year olds amongst females, with communicable causes contributing to three of the top five causes amongst males. HIV/AIDS and STI has been the leading cause group in this GBD super-region amongst females since the early 1990s in 15-24 year olds, and since the early 2000s in 10-14 year olds.

In Central Europe, Eastern Europe and Central Asia, self-harm has risen from 3rd highest cause of death in 1980 to be the leading cause of death amongst males 15-24 (now contributing to more than 20% of all deaths), and from 4th highest to the leading cause of death amongst females 15-19 and second highest cause amongst 20-24. Further, in 10-14 males, self-harm is now the 4th highest cause of death in this super region, causing almost 9% of all deaths. In

contrast, in Southeast Asia, East Asia and Oceania, self-harm amongst females 15-24 has fallen from the leading cause of death in 1980 with around 15% of all deaths, to 6th highest (15-19) and 7th highest (20-24) in 2019, (around 7% of all deaths in both age groups). In the High Income GBD super-region, deaths due to substance use disorders in young adults are also notable, rising from around 1% of total deaths in 20-24 in 1980 to between 14-16% (3rd highest cause in males and 4th highest cause in females) in 2019 in both sexes, with substantial increases also seen in 15-19.

Mortality in young people and socioeconomic development

Increasing SDI in 2019 was strongly associated with lower all-cause mortality rate per 100 000 for 10-14, 15-19 and 20-24 (see supplementary material 3 part a, table S3). Figure 66 (p.290) shows the ratio of observed to expected years of life lost (YLL) by SDI from all causes for 15-19 in 2017 (both sexes), with figures for 10-14 and 20-24 shown in supplementary material 3 part a, in addition to estimates from 1990 – 2017 for all countries (figures S26 – S49). Observed YLL from all causes in 15-19 was at least 20% higher than that which would be expected by SDI in 41 countries, including both Brazil and Pakistan which collectively contribute to around 10% of deaths in this age group. Amongst 15-19, the ratio of observed to expected YLL in 2017 was highest in Syria (4.02), however from 1990 to 2010 (prior to the start of the civil war), observed YLL in Syria were consistently around 30% lower than expected by level of SDI. 84 countries had observed YLL amongst 15-19 at least 20% lower than expected by level of SDI. The countries with the lowest ratio of observed to expected YLL in this age group were the Maldives (0.30), Spain (0.33) and Singapore (0.35). Other notable countries included China (0.49) and Ethiopia (0.67), (where around 7% of deaths in 15-19 occur).

Mortality in young people compared with early childhood

Annual percentage decline in mortality rate per 100,000 between 1990 and 2019 in infants (<1), 1-4, 5-9, 10-14, 15-19 and 20-24 year olds by sex, country and globally is shown in figure 67 (p.291). Rates of decline have been highest in 1-4 and lowest in 15-24 year olds. Amongst 1-4 year olds, global mortality rates have declined by around 2.4% per year since 1990 in both males and females, compared to rates of decline in 15-19 year olds of 1.3% in males and 1.6%

in females. The range in mortality rate change between countries was also greater in adolescence than in younger children (see supplementary material 3 part a, figure S24).

There is also variability within countries in terms of current mortality rate performance for different age-groups, particularly amongst males. Demonstrating this, figure 68 (p.292) shows mortality rate percentile for under 5s against 15-19 for each country in 2019 amongst males, with the equivalent figure for females shown in supplementary material 3 part a (figure S25). Although for most countries the mortality rate percentiles for these age groups are comparable, there are notable exceptions. For example, male under 5 mortality rates in Brazil and Venezuela are around the 60th centile globally, but above the 90th centile for 15-19 mortality. Similarly, Ukraine and Thailand have under 5 mortality rates around the 30th centile (best third globally), but 15-19 mortality above the 75th centile (worst quartile globally). In contrast, India has a mortality rate for under 5 year olds which is on the 70th centile, and a mortality rate for 15-19 year olds between the 30th-40th centile globally.

Figure 69 (p.293) shows the proportion of global deaths in the early life course (0-24) occurring in adolescence and younger children. The size of each chart is proportional to the total number of deaths in that year in 0-24. The figure shows the proportion of deaths occurring in 10-24 year olds has increased from 9.5% in 1950 to 21.6% by 2019. The proportion of deaths in 0-24 year olds occurring in young people increased in all GBD super-regions of the world between 1950 and 2019, with the greatest change seen in Latin America and the Caribbean amongst males, increasing from 7.5 to 39.2%. In the High Income GBD super-region, deaths in adolescence now account for more than half of all mortality in 0-24 year olds. In 9 countries, more than 70% of 0-24 deaths amongst males now occur in adolescence (Estonia, Thailand, Saudi Arabia, Finland, Puerto Rico, Slovenia, Monaco, Cook Islands and Andorra).

Figure 66: Ratio of observed to expected years of life lost (YLL) by SDI from all causes in 15-19 year olds in 195 countries in 2017 (both sexes)

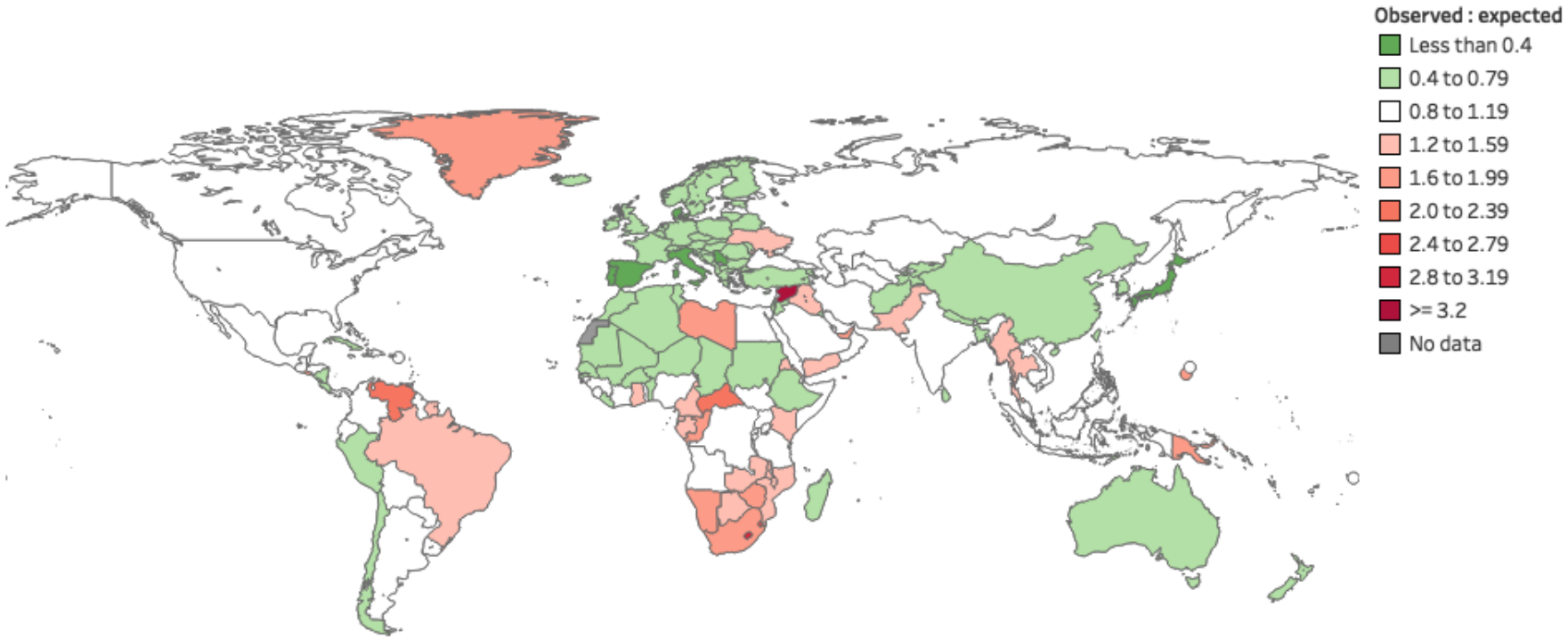


Figure 67: Annual percentage change in mortality rate per 100,000 between 1990 and 2019 in 204 countries and territories in infants, 1-4, 5-9, 10-14, 15-19 and 20-24 year olds by sex and GBD Super-Region

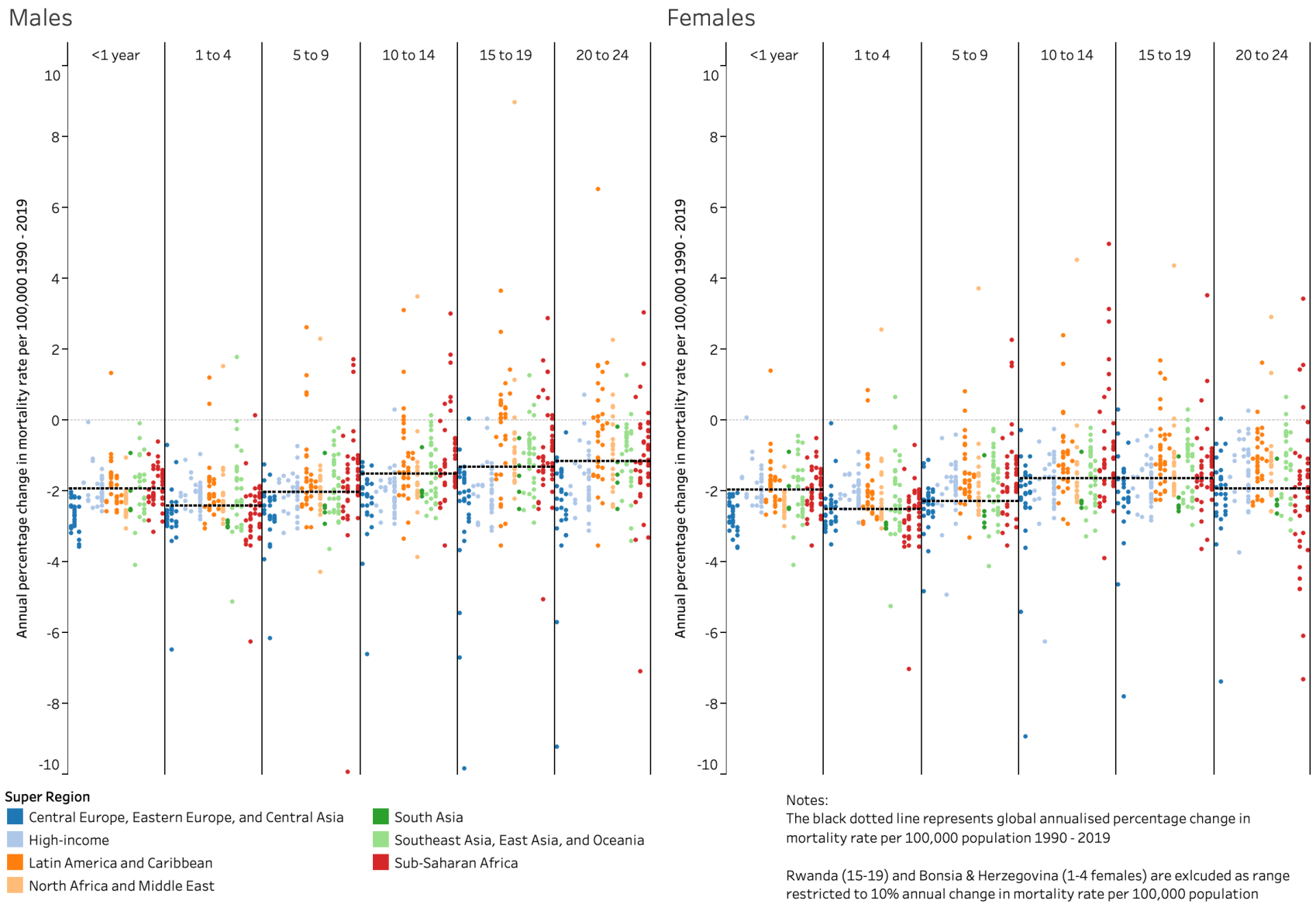


Figure 68: Mortality rate per 100,000 percentile for 0-5 against 15-19 year old males in 195 countries by GBD Super-Region in 2019

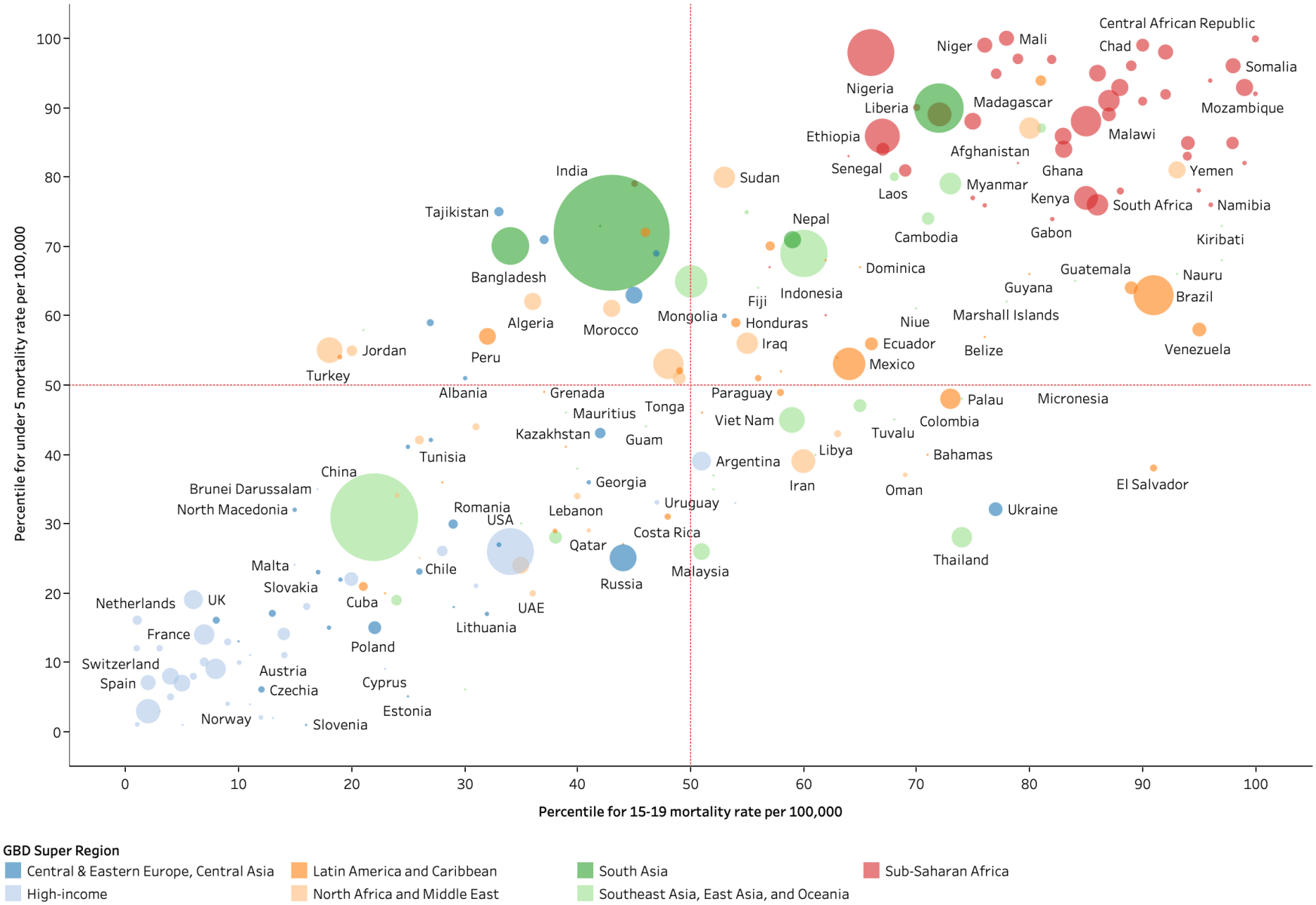
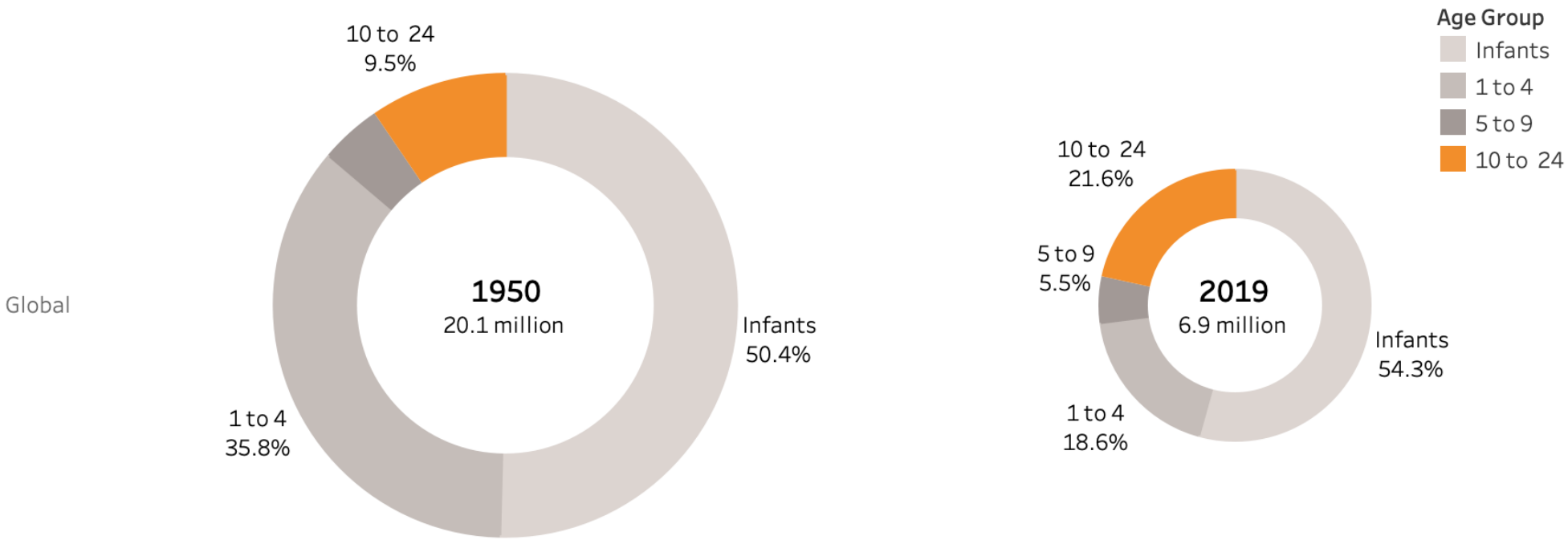


Figure 69: Proportion of global deaths in 0-24 year olds occurring in adolescents (10-24) 1950 and 2019 in both sexes



Chapter 9 discussion

Despite marked reductions in total numbers of deaths and mortality rates for young people aged 10-24 over the past 70 years, global improvements have lagged behind those seen in younger children, variation in outcomes between countries has increased, and inequities by sex have worsened. Global numbers of deaths in 10-24 year olds remain high, with around 4000 young people dying each day, mostly from preventable causes.

I found widening variation in all-cause mortality in 10-24 year olds between countries, particularly during early adolescence, and huge differences in the leading causes of death between different regions of the world, as others have shown.[338,346] Variation in all-cause mortality between countries appear likely to further increase, as population growth in this age group is highest in countries with the worst mortality outcomes (see supplementary material 3 part a figures S21-S23). Currently around 20% of 10-24 year olds live in sub-Saharan Africa, and this is set to rise to a third by 2050.[329] This presents real challenges to improving adolescent mortality. Of the ten countries with the highest mortality rates in 10-24 year olds in 2019, eight are in sub-Saharan Africa, and declines have been far slower than in other GBD super-regions. These changes are shifting the global burden of adolescent mortality towards sub-Saharan Africa, where 29.0% of deaths in 10-24 year olds now occur, compared with 8.1% in 1950. Sub-Saharan Africa has already replaced South Asia as the main contributor to global deaths amongst males 10-19, and is set to do so for males 20-24 and females 10-19 if current trends continue.

I found marked sex differences in adolescent mortality, with young men suffering notably higher mortality and having slower rates of decline than young women. Indeed, globally more adolescent males died in 2019 (910 000 [847 000 - 974 000]) than adolescent females in 1950 (831 000 [809 000 – 895 000]). Inequalities in mortality by sex also appear to be widening in many regions of the world. These differences reflect the increasing burden of deaths due to injuries and violence in this age group, particularly in Latin America and Caribbean, and the rise in deaths due to substance use in High Income settings, which predominately affect young men. Addressing inequities in access to health services and the social conditions in which young women live, and understanding the impact of gender-based violence, is fundamental

to improving adolescent health globally, and has understandably been the focus of previous programming.[341] However, inequitable gender norms are also damaging to adolescent males, and advancing the health of all adolescents requires action to reduce inequities in outcomes wherever they occur.

Consistent with previous studies[337,338,340,346], I found declines in adolescent mortality to have been slower than in younger children, particularly amongst males, with 1-4 year olds experiencing almost twice the annualised rate of decline than 15-19 year olds since 1990 in males, and around 50% higher in females. A previous analysis of long term mortality trends using WHO estimates found differences in mortality reduction by age resulted in 15-24 year olds replacing 1-4 year olds as the age group with the highest mortality burden in many countries.[337] 15-19 was also recently highlighted as the age group with the slowest mortality declines amongst 0-19 year olds using GBD data,[346] and Masquelier and colleagues found mortality declines in 5-9 year olds to exceed those of 10-14 year olds between 1990 and 2016 using estimates from the UN.[340] The continued neglect of this age group is highlighted by several mostly middle income countries such as Brazil and Mexico having relatively good outcomes for 0-4 year olds and persistently high adolescent mortality (figure 68, p. 292), suggesting more adolescent specific interventions are needed in these settings. Inequalities in the rate of improvements between age groups has transformed the global burden of mortality during the early life course. Almost a quarter of deaths in 0-24 year olds now occur during adolescence, with this proportion having more than doubled since 1950. Among High Income countries this rises to more than 1 in 2 deaths, and in countries of the world with particularly high mortality due to violence, adolescent deaths now account for up to three quarters of early life course mortality.

Meaning and mechanisms

This poor progress in reducing mortality may reflect the omission of adolescents from the majority of global health investments. Adolescents were largely absent from the Millennium Development Goal (MDG) agenda, and although will have benefited from public health interventions aimed at other groups, have not had the accelerated mortality declines seen in infants and younger children attributed to MDG programming.[346] The SDGs include indicators

which are highly relevant to young people, but do not provide a comprehensive mechanism to address the unique health needs of this age group.[346] Even defining a list of metrics to best capture global adolescent health priorities is yet to be established.[347] The 2016 Global Strategy for Women's, Children and Adolescents' Health and other initiatives have increased recognition of the crucial role of adolescents to the sustainable development agenda and global targets for Universal Health Coverage (UHC).[4] Yet investment levels remain inadequate, and specific challenges to improving adolescent health outcomes and achieving the core UHC indicators in this age group continue to be overlooked.[332,333]

These factors are compounded by limited evidence for effective adolescent health interventions needed to inform investment.[348] A key focus to improve outcomes in this age group should be to address these knowledge gaps to better establish which interventions work, guided by identifying and measuring key indicators which capture adolescent health priorities.[347] Investment in existing evidenced-base actions to prevent causes of death which predominate during adolescence is also likely to improve outcomes, but is currently inadequate. This should include improving water safety and unintentional injury prevention,[349] and targeting key behavioural, legal and structural risk factors for road traffic deaths.[350,351] Yet global increases in injury prevention spending have been lower than those on other public health interventions,[352] and progress towards reducing road traffic deaths in line with SDG targets is currently insufficient.[350] Self-harm has emerged as a leading cause of adolescent mortality, and now accounts for around 20% of all deaths 15-24 in the High Income and Central Europe, Eastern Europe and Central Asia GBD super-regions, and is the leading cause of death in South Asia for 15-24 females and second highest cause in 20-24 males. Although understanding these trends is complex and solutions to improve outcomes need to be country-specific, investment in evidenced-based interventions to improve mental health in this age group,[353,354] and measures to restrict access to firearms and chemicals used in suicide, are likely to be beneficial.[355,356] Yet global improvements to the quality and accessibility of mental health services has been slow, disproportionately affecting adolescents and young people.[354] Further, strategies to improve outcomes for communicable and maternal causes of death, which still contribute to around a third of global deaths in 10-24 year olds, need to be specifically tailored for this age group, as variation in adolescent HIV/AIDS mortality trends compared with older age groups demonstrates.[357] Although

evidenced-based interventions around adolescent sexual and reproductive health are available, these are mainly focused on high-income countries, and important evidence gaps remain.[358]

I found multiple large spikes in mortality over the study period, particularly in older male adolescents, as a result of violent conflict and natural disasters. Deaths due to interpersonal violence are also driving poor progress in reducing male all-cause mortality in many countries, particularly in Latin America and the Caribbean where there has been almost no improvement in all-cause mortality amongst 15-24 males over the past 20 years, with mortality rates increasing in many countries. Global strategies to improve adolescent health outcomes must include efforts to mitigate the effect of interpersonal violence and conflicts on young people. Existing humanitarian response guidance does highlight specific vulnerabilities of adolescents during natural disasters and conflict.[359] However, the evidence base to manage these in low and middle income countries remains weak,[360] and further work is required to understand adolescent health needs in these situations.

Reducing mortality in young people also requires an understanding of the broader social determinants of adolescent health, and how structural changes such as rapid urbanisation and technological and economic development may impact young people differently from other age groups. The importance of primary education to population health is well described, but national progress in secondary education is also associated with large improvements in all-cause mortality and other important health outcomes for young people.[361] The increasing numbers of adolescents growing up in urban settings may extend opportunities for education, in addition to potential economic benefits for young people and their families. However, rapid, unplanned urbanisation can also increase health risks which are pertinent to adolescents, including those related to injury, separation from family support through migration, exposure to violence, substance misuse and unsafe employment.[41,362] The effect of other macro-level health determinants appears to differ across the early life course, with national wealth a weaker predictor of adolescent mortality than it is in young children.[363] Indeed, for some common causes of death in adolescents (i.e. road injuries), rapid economic growth can actually result in a transient increase in mortality, as the introduction of safety legislation and appropriate infrastructure may lag behind rising demand for

transportation.[364,365] In contrast, inequality in income distribution within countries appears to be pervasively harmful throughout the early life course, and thus may be of greater relative importance to outcomes during adolescence.[363]

Strengths and limitations

I used the only available data source providing regularly updated mortality estimates for 204 countries and territories in 10-24 year olds by cause, and describe long term trends over time. These data are limited by factors inherent in production of GBD mortality estimates. The availability of authoritative mortality data for adolescents remains limited. Global coverage of civil registration systems is of varying quality, and progress to improve these systems has been minimal.[161] Primary data sources for adolescents are particularly scarce, as attempts to develop alternative methods to measure mortality have focused on other groups.[339] Data availability and accuracy will be further impeded by ongoing conflicts in many countries, and associated migration. Where data are available, there are often long time-lags in reporting outcomes. Analysing the global adolescent mortality burden is subsequently reliant on using modelled data, and the estimates I report here need to be viewed within that context. Limitations within the GBD estimation process, and the paucity of mortality data for this age group, is reflected in wide uncertainty intervals for many time periods, locations and causes of death I report here.

Using alternative data sources with different modelling techniques to the GBD may have resulted in differences to our results. Estimates for global number of deaths in 10-24 year olds in 2019 produced by the UN Interagency Group for Child Mortality Estimation were between 8-19% higher than the GBD 2019 (see supplementary material 3 part a, figures S113 – S115), and between 10-20% lower than those in World Population Prospects report.[342] Although variation in available mortality estimates for High Income countries have been highlighted,[191] the main discrepancies are within sub-Saharan Africa, where the future global burden of mortality in 10-24 year olds will be concentrated. This further highlights the need to expand primary data collection for adolescent health outcomes in this region.

I used SDI to identify countries with lower or higher adolescent mortality than would be expected from country income per capita, years in education and fertility under 25; indicators for socioeconomic development which are particularly relevant for adolescents. However, using other disaggregated metrics of development may provide additional insights, and further detailed analyses are required to explore the contribution of trends in key social determinants on adolescent mortality, which are likely to vary in different regions of the world. I reported estimates at the country level, and future analyses of adolescent mortality should include sub-national trends. Where these are available within GBD they demonstrate wide variation in outcomes, as demonstrated in Chapter 5 of this thesis. Using level 2 of the GBD cause of death hierarchy allows a description of high-level trends in mortality in young people, however further analyses using more granular cause of death data are needed to increase understanding of the patterns I describe. Analysing associations between healthcare quality and adolescent mortality using the Healthcare Access and Quality Index[366] provided by the GBD may also provide further insights, and looking beyond mortality and describing key trends in morbidity amongst young people, should also be the focus of future study.

Conclusions

I found global improvements in 10-24 mortality have been slower than in younger children. This and demographic change has more than doubled the proportion of deaths in 0-24 occurring during adolescence globally since 1950. There is wide variation in outcomes between countries, and progress amongst male adolescents has been particularly poor. These results reflect concerns regarding adolescent mortality in the UK highlighted in previous chapters. They point to persisting failures by policymakers both globally and in the UK to adequately address specific vulnerabilities and risk factors for death during the adolescent years, or respond to changes in the burden of early life course mortality.

The case for investment in this age group is compelling. To do so builds on health improvements achieved in younger children, will affect future adult health trajectories and those of the next generation,[328] and will be an important determinant of future economic development.[41,338,367] A renewed emphasis on reducing inequities in outcomes in this age group, improving the availability and quality of primary data, and establishing mechanisms to

use these data to better inform global health policy, focusing on regions of the world where mortality is increasing, is urgently required.

I will further explore how global trends described here may inform strategies to improve UK mortality in 1-24 in the next chapter, as I discuss the key findings of this thesis, limitations to the methods used, meanings, mechanisms and policy implications of my findings, how these may inform future analyses of UK CYP mortality.

Discussion

Summary of key findings

The results presented in this thesis identify multiple areas of concern regarding patterns of deaths in CYP in the UK. These offer possible explanations regarding the UK's high mortality compared with the EU15+, and identify areas to prioritise in order to improve outcomes.

Trends in CYP mortality described in Chapter 3 demonstrate remarkable progress in reducing deaths, with all age groups enjoying relative reductions in mortality rate of at least 60% since 1950. However, this analysis also confirmed that progress has been unevenly distributed by age group, with young children enjoying far greater reductions than adolescents. More recent trends are even more concerning for 10-24, with improvements stagnating since 2011 for many of the leading causes of death in this age group.

Chapter 4 showed all-cause UK CYP mortality declines since 1970 to be slower than the EU15+ median in all age groups and both sexes. Forecast trends described in this chapter suggest the UK is set to fall further behind for mortality in young children, and lose its position of having lower mortality in adolescents, by 2040. These international comparisons of all-cause UK CYP mortality conceal cause-specific variation in outcomes relative to the EU15+. I found current mortality for neurological, respiratory, diabetes/endocrine and common infections to be significantly higher in the UK than EU15+, but good outcomes for injury. However, I also found some evidence that the UK's position for injury deaths may be eroding.

Analyses demonstrating excess CYP deaths in the UK may partly be explained by areas of the country with particularly high mortality. In Chapter 5, I found marked variation in outcomes within the UK, with much of the south of England having lower mortality than the EU15+. This chapter also demonstrated wide variation in mortality for the causes of death where the UK as a whole performs badly, and large differences in outcomes amongst adolescents and young people, further adding to concerns regarding mortality in this age group.

In Chapter 6, I showed that much of the geographic variation in mortality in England can be explained by levels of deprivation, and found strong social gradients in mortality across all CYP age groups. Population differences by age and ethnicity are also likely to contribute to variation in outcomes, but do not explain all observed variance, particularly in older CYP. Although the most deprived local authorities tended to have higher CYP mortality, there were notable exceptions, particularly in London and other large cities. I also found the proportion of variance explained by clustering within English region varied with age, after adjusting for deprivation, age structure and ethnic differences. This might reflect socioeconomic and demographic factors which I did not capture in this analysis, but also differences in the effectiveness of public health services within England and, potentially, healthcare factors.

In Chapter 7 I describe large changes to emergency healthcare activity in England, including within causes where the UK has high mortality. I found admission rates of emergency care to be rapidly increasing, and separate analyses found much of this activity is due to conditions which could be managed in primary care.[283] There are multiple explanations for these trends, but they do further suggest that integration across parts of the health service could be improved. These factors directly relate to healthcare patterns I found to be associated with increased mortality hazard in Chapter 8, where recurrent admissions, missed appointments, contact with mental health services, and prolonged time to transition to adult care, were all associated with increased risk.

Most UK CYP deaths outside infancy occur in adolescents and young adults, where progress in reducing mortality has been slow, wide subnational variation exists in outcomes, and steep social gradients persist. However, analyses of global trends in mortality in 10-24 in Chapter 9 suggest factors contributing to poor mortality progress in this age group are not confined to the UK, and reflect broader concerns around the neglect of adolescent health priorities in both high and low-income settings.

Meaning, mechanisms and policy responses

Determinants of health, optimal development, and survival are complex and range from political, socioeconomic, and environmental determinants, through to population level public

health, to health system factors, individual behaviours and healthcare interactions. Strategies to address the UK's poor international performance for CYP mortality should therefore include action across all these domains. This includes considering how healthcare, public health and health systems may be improved to address the changing health needs of CYP, but also considering multiple other upstream determinants patterned by government and civil society.[13] Interventions also need to target the processes through which health inequalities described in this thesis arise and are perpetuated, and provide support that is proportional to need.[368]

Huge global differences in adolescent mortality I describe in Chapter 9 illustrate the strength of associations between national wealth and CYP mortality. However, as the UK and EU15+ are all high income countries, how income is distributed is likely to be a more important macro level determinant of international mortality differences within this group;[369] EU15+ countries with low mortality tend to be those with lower levels of income inequality. Further, the UK has higher levels of material deprivation than the best performing EU15+ countries,[268] and policies targeting poverty reduction amongst CYP are likely to be beneficial. Despite this, there are concerns that material deprivation in the UK is rising amongst CYP, and that increasing numbers of families are unable to provide basic items required for CYP health. Child Poverty Action Group estimate that child benefit has lost around a quarter of its value since 2010,[370] and the demand for food banks in the UK has rapidly increased over the same period, with further increases noted during the COVID-19 pandemic.[371] There is also evidence that recent reductions to welfare programmes in the UK have had the greatest effect on the most vulnerable, such as those with large families and children with disabilities.[45,372] Other macro level determinants include the impact of education on CYP health, shown to be strongly associated with improved health in multiple analyses.[361,373,374] Differences in educational attainment by deprivation are likely to compound existing health inequities, and policies aimed reducing these are likely to improve UK CYP mortality.[45] At the intermediate level, ensuring that universal public health measures are adequately funded and implemented is essential to CYP mortality,[45] and recent reductions in local authority funding levels risks impeding progress.[375,376] At the individual level, personal, family, and community conditions are strongly affected by the distal factors described above, but some may also be

realised through health behaviours. Policy responses to these should be considered in the context of wider social determinants.

Actions to reduce mortality risk in CYP also need to acknowledge that exposures are unevenly distributed, and congregate around families from lower social positions.[24] In order to successfully address inequities in CYP health outcomes, interventions should proportionately target those with most need.[377] This may include targeted interventions for deprived populations to improve the quality of housing, factors related to nutrition, the built environment and the neighborhoods in which CYP live and play.[45,378-381] In addition to differential exposures, CYP from deprived backgrounds are more vulnerable to specific risks, due to the accumulation of mortality risk factors amongst deprived populations. Social stratification due to structural factors, increased exposures and increased vulnerability, both increases the likelihood of ill-health amongst deprived CYP, but also effects the consequences of illness. These include financial consequences of caring for a child with increased health needs. For example, having a child with a long term illness or disability has been shown to be associated with reduced employment opportunities for parents.[382] However, differential consequences of illness also relate to how responsive health services are to the additional needs of CYP from deprived backgrounds. Although access to care in the NHS is equitable relative to many other countries, financial barriers to healthcare do exist. These include the cost of transport for appointments, and medical equipment or home alterations required for CYP with complex needs.[246] Policy to address these factors will improve outcomes for the most vulnerable CYP, and reduce inequities in mortality described in this thesis.

Health service factors

A high quality, accessible, and equitable health system is an important determinant of health and survival.[271] As discussed previously, a large proportion of CYP deaths in the UK are thought to be amenable to healthcare, and health service factors were identified in 35% of deaths with available data reviewed by the National Child Mortality Database in 2019.[383] There is some evidence that rates of avoidable mortality in the UK are higher than in many EU15+ countries,[270] and healthcare factors may be particularly pertinent for conditions where UK CYP mortality is high; it is estimated that there are avoidable factors in two thirds of UK

deaths due to asthma[273] and a quarter of deaths in children with epilepsy.[384] Many recommendations to improve asthma mortality in the UK relate to health service delivery,[80,272,273] and there are ongoing concerns about the quality of UK health services for CYP with epilepsy.[322] There are multiple other factors to consider with regard to health care quality in the UK which are difficult to measure or compare internationally, including how readily services can adapt to changes in the evidence base, understanding the experiences of those who access services, and the healthcare delivery needs of specific CYP.[385]

Education, training, and workforce numbers for children's healthcare professionals are important aspects of the health system, and may help explain country-level differences in survival. A recurring factor identified in CYP deaths is the failure to recognise serious illness by health professionals not trained in paediatrics,[44] yet there is no mandatory training in paediatrics for primary care practitioners in the UK, who provide the majority for healthcare needs for CYP.[44] Indeed, fewer than half of General Practitioners (GP) complete postgraduate placements in paediatrics, and undergraduate exposure is limited (4-6 weeks).[386] Yet plans to increase exposure to paediatrics for GPs in training have not been implemented. This is in contrast to the best performing countries for CYP mortality within the EU15+, where access to teams of paediatric trained healthcare professionals in the community is the norm.[279] A failure to provide sufficient sustained investment in policy and practice (and its evaluation) supporting inter and intra-sectoral cooperation in the UK has hindered necessary reforms.[279]

Another contributory factor to the UK's poor mortality performance may be related to healthcare organisation. There is concern that UK health services have been slow to adapt to the changing burden of disease in recent years, away from infectious causes to NCDs and mental health (the epidemiological transition).[13,192] Increases in chronic illnesses and long term conditions in CYP (such as asthma, diabetes and epilepsy) require a greater emphasis on primary care and public health interventions including health promotion and disease prevention. However, the UK’s predominately hospital-centric model of service delivery still focuses heavily on reactive acute and urgent care, and coordination between primary and secondary care in the UK continues to be worse than in comparable countries.[245] Fragmented clinical care and poor integration of different healthcare teams looking after children with asthma has been highlighted as a factor in preventable deaths deaths,[272,273] and sharp rises

in emergency admissions shown in Chapter 7 point to poor coordination between different parts of the healthcare system.

The need for better integration of paediatric services within communities, and across non-health sectors such as education and social care, is well established. These models of care have been adopted in the best performing countries for CYP mortality in this analysis.[279] As discussed in Chapters 7 and 8, improved integration of health services across multiple domains may address rising levels of emergency care admissions among CYP, and enable those at most risk of death to be better identified.[66] Improvements to integration have also been highlighted in recent recommendations to improve epilepsy care in the UK,[322] and address contributory factors in deaths due to asthma,[272] and other causes.[45]

Encouragingly, the NHS Long Term Plan in England,[21] and similar strategies in devolved nations, presents real opportunities to improve integration of services[45] through developing "integrated care systems" supported by *population health management* solutions. This refers to using large national data to guide health service improvements and population health, using methods similar to those I use in Chapter 8.[387] Part of this includes expanding the availability of deidentified linked data across health and non-health sectors, which will allow more sophisticated analyses needed to identify CYP at most risk, and inform areas where integrated care may improve outcomes.[21]

However, introducing a comprehensive integrated health service model will require action at all levels of health determinants, including upstream social factors and those related to non-health sectors. There are multiple challenges to realizing these ambitions, due to their complexity and investment requirements. Providing robust evidence to support the effectiveness of different integrated care models will be essential to this, as will additional support to increase health strengthening research capacity for CYP.[66]

Strengths and limitations

Strengths of these analyses include the broad range of datasets and methods I use to explore UK CYP mortality to aid understanding of international mortality differences. I analyse current and previous trends in CYP mortality by cause at population level, use forecast data to assess

likely future trends, and analyse subnational variation in outcomes in detail. Securing access to individual death certification data for England and Wales allowed for an analysis of variation in mortality by family / individual occupation, and to describe variation in death registration delay by cause of death and age, not available using publicly available datasets. I use hospital administrative data to describe trends in healthcare activity, developing novel methods to characterise admission by cause, and perform survival analyses of cohorts of CYP admitted with conditions where the UK performs poorly. Finally, I use GBD data to place concerns around UK trends in adolescent mortality in a global context, describing current patterns and long term trends in mortality in 10-24 in 204 countries and territories.

Where possible, these analyses use death registration data to estimate current and previous mortality burden, and compare these internationally. In countries with complete registration systems, such as the UK and EU15+ countries, death registration data can be considered the gold standard for mortality analyses at population level. However, although the UK has one of the highest quality death registration systems globally,[160,161] there are multiple shortcomings to death coding, and reform of these processes in the UK which may affect estimates presented in this thesis.[13,44,132-134,136,137,146,147] There are also large differences internationally in these systems, including within countries in the EU15+, which should be considered when interpreting these results. Differences in the way countries compile mortality statistics, and whether deaths are reported by registration year or death year, may have impacted my results, particularly for recent data years.[204] Cause of death analyses are complicated by the use of inappropriate and poorly coded of cause of death ("garbage codes").[188,189] I used modified GBD methods to redistribute these, which can have a large impact on mortality estimates both in the UK and internationally; using other approaches to deal with these codes may have had substantial impacts on my results.

I used modelled mortality data from the GBD study in this thesis to complement analyses using death registration data only. Strengths of GBD data include the standardisation of registration data from multiple sources, allowing cause specific differences in mortality across different iterations of ICD to be analysed, the availability of estimates at granular geographic level (i.e. by English local authority), and estimates for data poor countries. However, these

are limited by the GBD estimation process, and there can be large differences in estimates compared with other datasets, including for high income countries.[191]

The national reach of HES data allowed for population level analyses of healthcare activity in Chapter 7, and survival analyses in Chapter 8, of large cohorts of CYP with chronic conditions. However, as I describe previously, these data are subject to a number of limitations, and data quality, completeness and accuracy are variable.[165,174-183] Linking these data with other sources, for example critical care datasets, mortality data not solely based on registration, and most importantly primary care data, would improve these analyses.

This analysis does not include the impact of the COVID-19 pandemic on CYP. Young children appear to be less susceptible to SARS-CoV-2, although this is similar to older groups for adoelscents.[388] However, case fatality has been much lower than in older adults,[334,389] and the direct effect on mortality in CYP is likely to be small. More concerning are the indirect effects of COVID-19 on health, particularly through disruption to health services caused by the pandemic, the impact on opportunities for education and employment, and the exacerbation of existing inequalities.[390] Further, adolescents and young people are more likely to work in sectors vulnerable to restrictions introduced during pandemic than older adults, and are at greater risk of losing employment and reporting reduced earnings.[391] There is some evidence to suggest young people have been more affected by worsening mental health than older adults, and even concern that suicide risk in early adolescence may have increased.[392,393] Broader effects of the pandemic to key CYP health determinants are likely include those related to economic instability, and failing to prioritise the climate crisis.[394] The extent to which these impacts will effect well-being in CYP, and prospects to improve health outcomes including mortality, are not understood and warrant further study.

Future directions and next steps

Important next steps to this analysis should be to explore other population level datasets on important aspects of CYP health service use. This should include exploring patterns of healthcare activity in primary care data, where the majority of CYP health problems are managed. These data are fundamental to understanding patient pathways from the

community to hospital admission and outpatient services, and in identifying patients who are at greater risk of death. Within the hospital data I have used, I have not been able to include complete analyses of mental health services, nor of admissions to critical care, as data completeness for these datasets is variable. Understanding how contact with mental health services, and barriers to this, interacts with risk of death in CYP with chronic diseases, and of how prior admission to critical care predicts future mortality, should also be the focus of future study. Although I have examined accident and emergency use, these data are crude and do not reliably provide detail on the reason for attendance, essential to identifying increased risk. Changes to the HES Accident and Emergency Dataset introduced in 2017 may provide opportunities to investigate this in greater detail. Further, although I have examined individual level hospital activity, I have not attempted to identify healthcare providers with higher or lower than expected mortality, a potentially important determinant of deaths in CYP.[62]

Establishing indicators to understand healthcare quality in the UK and other countries, which should go beyond observing patterns at population level and incorporate individual experience of healthcare, will be important future steps for this analysis. Within this there may be opportunities to examine the effectiveness of initiatives to improve quality, such as through improved integration of primary and secondary services, and then exploring if these are impactful at population level.

Conclusions

It is clear that there are complex interacting factors in the causal chain leading to UK's inferior CYP survival outcomes compared with EU15 countries. This also means that there are multiple policy opportunities to intervene. This should include addressing high and rising levels of material deprivation for CYP in the UK, ensuring preventative public health measures are adequately funded, and targeted interventions to address the uneven distribution of mortality exposures. There is also growing evidence that poor integration within the health service, and across non-health sectors, may be contributing to increased risk, particularly for CYP who are already vulnerable. As highlighted by the RCPCH, improvements across these determinants will require an overarching cross-government cross-country child health

strategy for the UK, and developing a child-health-in-all-policies approach to reduce health inequities.[12]

To further inform interventions, analyses are required to explore how multiple determinants for CYP health interact and result in variation in mortality risk for different causes of death. These should include examining how responsive primary and secondary healthcare services are to variation in risk, and the degree to which they are able to co-ordinate action to protect vulnerable CYP. Understanding how the COVID-19 pandemic has affected health outcomes for CYP in the UK also warrants further study. This should include investigating both direct and indirect impacts of the pandemic, using methods similar to those described in this thesis. Establishing routine linkage of Hospital Episode Statistics data with other datasets across different parts of the health system, and non-health sectors, will enrich these and other analyses of CYP health in the UK.

Finally, health systems and policy research, which is still underdeveloped for child health and in high income countries, can produce new knowledge helping us better to understand the causes of poor outcomes. Further, developing and evaluating ambitious policy and complex health system interventions, based on evidence from countries with better outcomes, will help us illustrate the pathway to improving UK CYP health and survival.

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